TRAINEE SECTION

Jodie I. Roberts
Jennifer K. Beatty
Michael A. Peplowski
Michael B. Keough
Bryan G. Yipp
Morley D. Hollenberg
Paul L. Beck

Proceedings from the 6th Annual University of Calgary Leaders in Medicine Research Symposium

Abstract

On November 14, 2014, the Leaders in Medicine (LIM) program at the Cumming School of Medicine, University of Calgary hosted its 6th Annual Research Symposium. Dr. Danna Skowronski, Epidemiology Lead for Influenza and Emerging Respiratory Pathogens at the British Columbia Centre for Disease Control (BCCDC), was the keynote speaker and presented a lecture entitled “Rapid response research during emerging public health crises: influenza and reflections from the five year anniversary of the 2009 pandemic”. The LIM symposium provides a forum for both LIM and non-LIM medical students to present their research work, either as an oral or poster presentation. There were a total of six oral presentations and 77 posters presented.

The oral presentations included:

- Swathi Damaraju, “The role of cell communication and 3D Cell-Matrix environment in a stem cell-based tissue engineering strategy for bone repair”;
- Menglin Yang, “The proteolytic activity of *Nepenthes* pitcher fluid as a therapeutic for the treatment of celiac disease”;
- Amelia Kellar, “Monitoring pediatric inflammatory bowel disease – a retrospective analysis of transabdominal ultrasound”;
- Monica M. Faria-Crowder, “The design and application of a molecular profiling strategy to identify polymicrobial acute sepsis infections”;
- Waleed Rahmani, “Hair follicle dermal stem cells regenerate the dermal sheath, repopulate the dermal papilla and modulate hair type”;
- Laura Palmer, “A novel role for amyloid beta protein during hypoxia/ischemia”.

The article on the University of Calgary Leaders in Medicine Program, “A Prescription that Addresses the Decline of Basic Science Education in Medical School,” in a previous issue of CIM (2014 37(5):E292) provides more details on the program. Briefly, the LIM Research Symposium has the following objectives: (1) to showcase the impressive variety of projects undertaken by students in the LIM Program as well as University of Calgary medical students; (2) to encourage medical student participation in research and special projects; and, (3) to inform students and faculty about the diversity of opportunities available for research and special projects during medical school and beyond.

The following abstracts were submitted for publication.

Proceedings from the 6th Annual University of Calgary Leaders in Medicine Research Symposium, November 14th, 2014.

Clin Invest Med 2015; 38 (6): E318-E350.

Abstract 1

The design and application of a molecular profiling strategy to identify polymicrobial acute sepsis infections

Monica M. P. Faria-Crowder^{2,4}, John M. Conly¹⁻⁴, Michael G. Surette^{2,4,5}

¹Departments of Medicine, ²Microbiology, Immunology & Infectious Diseases, ³Pathology & Laboratory Medicine, ⁴Snyder Institute for Chronic Diseases, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada; ⁵Farncombe Family Digestive Health Research Institute, Departments of Medicine and Biochemistry and Biomedical Sciences, McMaster University, Hamilton, Ontario, Canada

Background: Sepsis is a broad term used to describe a vast range of clinical presentations ranging from mild body dysfunction to multiple organ failure. These clinical signs are a result of a systemic inflammatory response to microbes or microbial products present in sterile sites such as blood. Current clinical diagnostics rely on culture techniques to identify systemic infections. However, culture lacks sensitivity and a positive result is only obtained in 40% of cases thereby limiting our knowledge of sepsis microbiology.

Methods: Disruption of blood cells with detergent and hypotonic shock was done to enhance recovery of the community. Efficiencies of recovery and limits of detection were determined for both viable cells and DNA using synthetic bacterial communities inoculated into whole blood. The method was applied to clinical samples collected from consented patients in both the intensive care unit (ICU) and emergency department (ED) from Foothills Medical Centre. Total DNA was extracted for bacterial community profiling using paired-end Illumina MiSeq sequencing of the V3 region of the 16S rRNA gene.

Results: Application of the paired-end Illumina 16S rRNA sequencing to saponin treated blood from ICU and ED patients indicated there were five common bacterial DNA profiles present in whole blood. These patterns were examined alongside the patient's clinical data and indicated common molecular profiling patterns correlated with the primary source of infection. Several case studies demonstrated the strength of molecular profiling to identify a principal pathogen that was not recovered using diagnostic blood culture. Bacterial DNA from *Streptococcus* and *Staphylococcus* were abundant in patients

that died in the ICU. Polymicrobial DNA was present in the majority of blood samples with the taxonomic profiles suggesting commensal microbiota were implicated in addition to a principal pathogen. As such, a role for reduced mucosal barrier function was also hypothesized to play a role in the presence of bacterial DNA detected in the bloodstream.

Conclusions: Overall, common bacterial DNA patterns were identified in the blood of septic patients in both the ICU and ED. These profiles were associated with the patients' primary source of infection, implicated the commensal microbiota in systemic infection, and suggested that certain bacterial DNA profiles were associated with mortality in the ICU. Taken together, molecular profiling could be used to identify bacterial DNA profiles that provided clinically significant findings, not observed with diagnostic blood culture, when interpreted in conjunction with patient admissions data.

Abstract 2

Hair follicle dermal stem cells regenerate the dermal sheath, repopulate the dermal papilla and modulate hair type

Waleed Rahmani¹, Sepideh Abbasi¹, Andrew Hagner¹, Jeff Biernaskie¹

¹Department of Comparative Biology and Experimental Medicine, Faculty of Veterinary Medicine, University of Calgary, Calgary, Alberta, Canada

Background: Dermal stem cells residing within the hair follicle mesenchyme have recently been identified and characterized as key multipotent cells that induce hair follicle growth and play a role in dermal maintenance. Moreover, the two dermal compartments of the hair follicle, dermal sheath (DS) and dermal papilla (DP), have been shown to express the stem cell gene Sox2 as well as generate skin-derived precursors (SKPs) when cultured. However, the primary source, migration pattern, and fate of these dermal stem cells remain a mystery. Here we hypothesized that α SMA+ dermal stem cells reside in the DS, regenerate the DS, and contribute cells into the DP.

Methods: To address this, we generated two inducible Cre-lox transgenic mice, α SMA-CreERT2:ROSA26^{eYFP} and α SMA-CreERT2:ROSA26^{confetti}, to perform in vivo genetic lineage tracing experiments. Tamoxifen treatment during early anagen (hair follicle growth phase) exclusively labeled DS cells and not

the DP. We then documented the fate of these cells over multiple hair follicle cycles for up to 7 months.

Results: Our results identify a population of bipotent self-renewing hair follicle dermal stem cells (hfDSCs) that envelop the telogen DP, are activated at the onset of anagen to regenerate the DS and are retained at the end of each hair follicle cycle. More importantly, hfDSCs are capable of contributing cells into the DP that are in turn capable of exiting the DP and re-entering the hfDSC niche after hair follicle degeneration.

Conclusion: This work provides definitive evidence for the existence and location of a dermal stem cell within the adult hair follicle and provides new insights into the lineage relationships within the mesenchymal compartment of the hair follicle. Moreover, since human clinical studies suggest that DP cell loss is the primary contributor to androgenetic alopecia, our findings have direct implications toward understanding the pathological mechanisms that underlie hair loss.

Abstract 3

A novel role for amyloid beta protein during hypoxia/ischemia

Laura A. Palmer¹ and Roger J. Thompson¹

¹Department of Cell Biology and Anatomy, Hotchkiss Brain Institute, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

Background: Alzheimer's Disease (AD) is a progressive neurodegenerative disorder that is associated with genetic and environmental risk factors, including stroke (ischemia). AD involves the formation of deposits of the protein amyloid beta (A β). Interestingly, basal levels of A β are upregulated under hypoxic conditions. During ischemic stroke, neurons lose their ability to maintain ionic gradients, which leads to ionic dysregulation known as the anoxic depolarization (aDP). The ion channel pannexin-1 (Pannx1) has been demonstrated to be integral to the aDP and is opened by *N*-methyl-D-aspartate receptors (NMDARs) through Src family kinases during hypoxia. We hypothesize that A β upregulation during hypoxia functions to protect brain tissue by interacting with Pannx1.

Methods: Whole cell patch clamp electrophysiology was used in hippocampal slices from rats, which were continuously perfused with hypoxic artificial cerebral spinal fluid in order to

mimic ischemia and induce the aDP. Various concentrations of A β protein were applied concurrently with hypoxia (pM to μ M range). In a separate set of experiments, slices were incubated in a γ -secretase inhibitor to decrease production of A β prior to application of hypoxia. Finally, low concentrations of A β were applied with a Pannx1 antibody, NMDAR antagonist, or Src inhibitor in order to observe if there are any additive neuroprotective effects of pharmacologically blocking these three targets in the presence of A β .

Results: Depletion of A β exacerbated the aDP, while application of low concentrations of A β attenuated the aDP. Interestingly, high concentrations of A β worsened the aDP. Concurrent application of A β and a Pannx1 antibody, NMDAR antagonist, or Src inhibitor was not additive on the effect of A β alone.

Conclusion: These data suggest that A β acts as a neuroprotective agent during hypoxia/ischemia by interacting with Pannx1 through NMDARs and Src. This gives insight into the physiological activity of A β and can provide better understanding of the underlying cause of stroke-induced AD.

Abstract 4

Unprofessional conduct in the health care profession: results from a qualitative study of disciplinary decisions against registered nurses in a Canadian province

Tracy L. Powell¹, Andreas E. Tomaszewski², Sydney M. Malenfant³, and Neil Zimmerman³

¹Department of Nursing, Mount Royal University; ²Department of Justice Studies, Mount Royal University; ³Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

Introduction: Misconduct in the health care profession costs lives and money. It can be directed at patients, co-workers, or employers. The conduct of members of the health care profession, like that of many other professionals, is self-regulated. Although a serious issue, little is known outside of the regulatory bodies regarding the extent and types of misconduct in this field and the effectiveness of sanctions.

Methods: We analyzed the content of publicly available data on complaints of professional misconduct against registered nurses (RNs) and the resulting disciplinary actions, paying par-

ticular attention to variables such as complainants, alleged offenses, victims, offenders, and settings.

Results: Preliminary findings. There were roughly two disciplined misconducts observed per discipline file (no gender difference[s]). 26% of the files are on men who make up 5% of the nurses in total. Thus, the number of disciplined misconducts were 5x higher for male than female nurses. The most common types of misconduct RNs were disciplined for are as follows: False documentation re client care (41/203); criminal conviction (22); negligent care (20); theft/fraud (19); drugs (18). Gender differences are as follows: Female nurse misconduct: false documentation (31/155); negligent care (20); theft/fraud (15); drugs (14); failed to assess client (14). Male nurse misconduct: criminal conviction (12/48); false documentation (10); theft/fraud (4).

Conclusion: The most common types of misconduct against patients that RNs were disciplined for included false documentation regarding client care and negligent care. Results have to be interpreted with caution as the data analyzed here only consist of incidents that were reported. Accordingly, the 'dark figure' of RN's professional misconduct remains unknown. An alternative might be to conduct a self-report study. In the absence of longitudinal data, it is also impossible to determine the effectiveness of arguably weak disciplinary action administered through self-regulatory approaches. Future research needs to examine the root causes for the misconduct and also explore whether male RNs are in fact committing more acts of misconduct or are subject to higher scrutiny in this female-dominated profession.

Abstract 5

"DOCS": Donor Offer Call Simulation; a novel tool to evaluate nephrology and kidney transplant trainees in managing deceased donor kidney offers

Monika Oliver¹, Kevin Wen², Hatem Alnasser², Allan Murray², and Sita Gourishankar²

¹Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada; ²University of Alberta, Edmonton, Alberta, Canada

Introduction: Competence in accepting deceased donor kidney (DDK) offers for transplantation is a curricular expectation of nephrology/transplant trainees. Yet the current curriculum dedicates minimal formalized training to the refinement of

this skill. We assessed trainees' competence in accepting DDK offers by reviewing their performance following participation in a Donor Offer Call Simulation (DOCS) exercise.

Methods: A standardized DOCS rubric was developed for the purposes of assessing participants' preparedness in accepting DDK calls. Seven categories, known to be relevant to decision making for organ allocation, graft outcome and acceptance or discard of an organ, were examined. One nephrology and two transplant trainees participated in two DOCS, typical of DDK offer. Two silent observers witnessed the simulations and scored participants using the DOCS rubric, with points awarded for probing and successfully acquiring key donor information.

Results: All three participants reported increased confidence and competence in participating in donor offer calls following completion of the DOCS. Mean scores for both simulation scenarios were 54.14% (Range 35.02%-79.9%, $p < 0.05$). Performance was correlated with level of training; with the two transplant fellows consistently outperforming the nephrology trainee ($p < 0.5$). Notably the transplant trainees at the end of the training year still missed between 25-50% of critical information.

Conclusions: DOCS identified important competency gaps in trainees for accepting DDK offer calls. This highlights the need for improved training practices implemented early in the nephrology-training curriculum. DOCS is a highly efficient and cost effective model that can be easily incorporated into current training practices. A potential exists to implement the DOCS scoring rubric into clinical practice to systemize the donor offer process thus ensuring complete information acquisition and enhance reproducibility between calls.

Abstract 6

Working under knifepoint – perceived abuse and intimidation of medical students

Jacob Charette³, Jill Stone^{1,2,3}, and Donald McPhalen^{1,2,3}

¹Division of Plastic Surgery, ²Department of Surgery, ³Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

Introduction: The progression from classroom to clinical setting can be a challenging transition for medical students. The

expectation and roles of medical students often vary between specialties. Experience in the operating room is anticipated as one of the most challenging environments for the novel medical learner. We sought to identify common concerns prior to exposure in this learning environment and examine the experience of final year medical students on their surgical clerkship rotation in an effort to identify areas where improvements can be made.

Methods: A twenty-question survey was developed after a focus group met to identify potential issues that medical students encounter during their surgical clerkship. Personal and anecdotal experiences guided the development of the survey. It was distributed to final year medical students and recent graduates (350 individuals) using SurveyMonkey. A quality improvement ethics application was completed prior to the commencement of the survey as were participant consent forms. Two investigators grouped responses and identified common themes in the experiences reported.

Results: Seventy-two individuals responded to the survey providing a 21% response rate. Subjects were asked how confident they were in their understanding of what was expected during a surgical rotation. Fifty-two (72%) responded that they were “unsure” or “very unsure” while only twelve and three felt “somewhat confident” and “very confident”, respectively. The majority of learners felt nervous (96%) and feared appearing incompetent (89%). Common concerns included insufficient knowledge and technical skill, anticipated negative experiences and feelings of uncertainty regarding medical student expectations.

Conclusion: We present common themes stemming from medical student experiences during their surgical clerkship. We comment on perception of intimidation and abuse, the rationalization behind such behavior, and perceived lack of guidance. The intention of this analysis was to identify weaknesses in our surgical training so that a quality improvement plan can be implemented.

Abstract 7

Rare diseases and orphan drugs in Alberta: The landscape and the liability

Sheila Acharya Van Horne¹

¹Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

Introduction: During the past 30 years, research, development and availability of innovative drugs to treat rare diseases have been enhanced globally. Many of these drugs have been priced high causing public and private insurers around the world concern. There are questions about the sustainability of paying high prices that consume large proportions of health budgets to the detriment of other areas of health care.

Methods: A scoping review was conducted to understand the extent of the orphan drug issue here in Alberta, Canada and globally. News articles, government websites, and peer-reviewed journals were reviewed to understand the approval process. Finally, a legal analysis was conducted to assess whether the current process in Alberta was fair and whether it placed the government at risk of liability.

Results: Unlike many countries, Canada does not currently have any orphan drug legislation. In 2012, the federal government announced that a framework would be put in place, however to date, nothing has been implemented. In Alberta, the government has implemented a *Rare Diseases Drug Program* (“RDDP”). The RDDP’s “Expert Committee” determines what drugs will be covered by the program, treatment guidelines and criteria for coverage. Some have deemed the process unclear and lacking in transparency, calling into question the fairness of the program and the potential legal liability to the government.

Conclusion: The threat of growing orphan drug costs to overall health budgets is real. Currently, there is no legislation in place in Canada or Alberta that addresses the subject. The RDDP in Alberta has turned its mind to the issue, however the lack of transparency and clarity around the decision-making process calls into question its fairness and poses a potential legal risk to the government.

Abstract 8

Health communities and inequity: A content analysis comparing the Google domains of Fragile X Syndrome and Cystic Fibrosis

Stephanie D'Agostini^{2}, Jacqueline Harrison^{2*}, Jennifer Mateshaytis^{2*}, and Lynn McIntyre^{1,2}*

¹Department of Community Health Sciences, ²Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

Introduction: The communication of health is sociocultural as is the communication of pediatric developmental disorders. Internet displays are important in communicating health needs, promising research, and fundraising goals to the public on behalf of a health community. The purpose of this study was to compare the web content available for two pediatric developmental disorders in order to discern and explicate differences that privilege one condition over the other.

Methods: In addition to sharing a similar prevalence, Cystic Fibrosis (CF) and Fragile X Syndrome (FXS) are life-long, incurable, multi-systemic and genetic conditions. Content analysis was simultaneously conducted on the top 30 links in the Google domain for each condition on two occasions. Coding of web content retrieved via standardized search queries addressed website category, content, target audience and tone.

Results: Significant differences were seen between CF and FXS. The average number of total hits for CF (23,500,000) exceeded FXS (2,085,000). CF was found to have a higher proportion of National Organizations ranking in the top 30 hits, whereas the majority for FXS was dedicated to health databases. CF was found to offer a wider variety of content, including information, event promotion, and programs and services; the majority of FXS's top 30 hits were solely informational. A subjective analysis of tone was performed for each disorder with high inter-observer reliability; 21/30 websites for CF depicted an overarching positive tone while 23/30 websites for FXS were neutral.

Conclusions: Although these disorders share many attributes, CF presents a more comprehensive and positive approach to the condition, while FXS focuses more on dissemination of neutral, disorder-related information. Inequities observed in these two health communities include disparity in resources and access to information for providers and affected families,

which are unwarranted and perhaps unfair given similar prevalences.

Abstract 9

Inequity amongst children's developmental conditions: marketing tactics in a crowded field

Stephanie D'Agostini^{2}, Jacqueline Harrison^{2*}, Jennifer Mateshaytis^{2*}, and Lynn McIntyre^{1,2}*

¹Department of Community Health Sciences, ²Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

Introduction: Evidence suggests that caregivers use the Internet to find information and resources for their child's health condition, yet web presence differs in its ability to effectively sell information and resources. This study compares the Google domain web content available for five pediatric developmental disorders in order to explore any differences in health information and service access.

Methods: Cystic Fibrosis (CF), Fragile X Syndrome (FXS), Down Syndrome (DS), Duchenne Muscular Dystrophy (DMD), and Spina Bifida (SB) were selected based on specific inclusion criteria. Content analysis was conducted on pre-set dates, using a coding sheet to consistently evaluate the Google domain content retrieved via standardized search queries. The top 30 links were ranked and evaluated.

Results: The disorders differed significantly with respect to total number of hits, website category and website content. DS and CF had 101,300,000 and 23,500,000 hits respectively; with the other disorders totaling less than 5,100,000 hits each. The predominant website categories were national organizations for CF and SB, local organizations for DS, and health informational databases for DMD and FXS. In a subjective analysis of tone over 65% of the websites for CF and DS depicted an overarching positive tone, while at least 50% of each of SB, DMD and FXS's hits were neutral. Of note, websites targeted the public as their audience as opposed to those affected by the condition.

Conclusions: Although these disorders share many attributes, they present vast differences in their web presence and content. CF and DS present a more well-rounded, positive approach to disease, while FXS, SB and DMD focus on dissemination of

disorder-related information. Physicians should be mindful that more activist disorders might receive inequitable attention from health care systems. Improvements to tools and information are necessary to provide reliable and useful online resources to families for FXS, SB and DMD.

Abstract 10

A problematic role of 'patient choice' in elective surgical decision-making

Shoghi Nikoo^{1,2} and Ariel Ducey²

¹Cumming School of Medicine, University of Calgary; ²Department of Sociology, Faculty of Arts, University of Calgary, Calgary, Alberta, Canada

Introduction: In response to criticisms of paternalistic medicine, respect for patient autonomy has become a central principle in ethical medical practice. A key part of this principle is emphasis on patients' right to choose their treatment course. If patients are able to choose which treatment is best for them, the argument goes, then the patient's perspective will be preserved. However, recent evidence suggests that shifting the responsibility for medical decision-making onto patients introduces new problems. The present research investigates how 'patient choice' acts in the medical decision making conversations in a clinic that provides elective urogynecological surgery.

Methods: This research utilizes results of ethnographic observations of interactions between surgeons and patients. The researcher shadowed surgeons for six weeks and produced detailed fieldnotes about the interviews, examinations, tests, and discussions observed. The conclusions here are based on themes and categories developed using common procedures for analyzing qualitative data. Data were coded using Nvivo 10.

Results: Decisions regarding whether to have surgery and which surgery to have often arose smoothly out of conversations between doctors and patients. In these encounters, 'patient choice' did not arise as a central issue; instead, options emerged in such a way that one appeared more desirable than the others. Other times, however, the best course of action was unclear. In these encounters, after some discussion centered on success and complication rates, surgeons would tell patients it is their choice and often have them leave the clinic to make their decision.

Conclusions: 'Patient choice' therefore shifts responsibility for the decision onto to the patient. Rather than encouraging surgeons and patients to share the work of decision-making, emphasis on 'patient choice' may isolate patients from surgeons, making more difficult the tough act of choosing whether to have surgery, especially when it is elective.

Abstract 11

Fielding's anatomy: Doctors, drink, and deformity

Veronique Ram¹

¹Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

Introduction: Literary criticism highlights how contemporary novels portray medical practices as metaphors for social control. In fact, during the late eighteenth century, the rise of scientific knowledge over religious discourse shifts the image of the body as God's vessel to one increasingly represented in clinical terms. Medicine, which continues to grow into an elite profession, emphasizes the need to diagnose and label extraordinary bodies in order to understand their physical error. Indeed, the paternalistic physician characters express anxiety over non-normative bodies, labeling them as social illnesses requiring isolation, for they disrupt social order. All bodies must assimilate to the proper body norm – one that proves legitimate and civilized – or else they trouble the universality of *the* human.

Methods: A literature review of databases (MLA Bibliography, Medline) was performed to explore previous research on doctors as literary characters, and to consider theories on the body, the nation, and the representation of medicine as paternalistic in literary texts. A summary of the results was drafted and included over 300 texts. After reading said texts, the literature review was narrowed to deformity in contemporary Canadian fiction (post 1960).

Results: I chose to focus on the Canadian novel, rather than non-fiction or poetry, because the genre remains historically recognized as one that provides a rich avenue for social commentary and questions of nationalism. My annotated bibliography includes 100 texts published since 1960 that include a physician character that plays a role in defining the normative and non-normative physical health of the nation. The data was subsequently narrowed to focus on 6 novels in which children

were the deformed figures intended as symbolic challenges of the medicalization of Canadian society.

Conclusions: For the purposes of this presentation, I focus on two novels, *The Colony of Unrequited Dreams* and the sequel, *The Custodian of Paradise*, in order to demonstrate how women's bodies, as a popular and potent metaphor, must remain healthy and meet normative expectations to act as vessels for the health of the nation. The main character, Fielding, is subjected to continuous incarcerations as a result of deviant drinking, disease, and deformity, which threaten the health of the nation. My central thesis considers such deviance, however, a contestation of paternalistic models of medical practices. Contrary to some critics, who perceive Canadian society as in a palliative state, subject to pharmaceutical care and the failure of the human body, I argue that deformity avoids a defining diagnosis.

Abstract 12

Correlations amongst mental health, cognitive flexibility, and zinc status

Emily Macphail¹ and Richard H. Dyck^{1,2}

¹Cumming School of Medicine, University of Calgary, Calgary; ²Hotchkiss Brain Institute, Alberta, Canada

Introduction: Cognitive flexibility impairment has been seen in both anorexia nervosa (AN) and commonly comorbid disorders, as have symptoms overlapping with those of zinc depletion. Risk groups for zinc depletion and AN also have distinct overlap, and zinc has been found to play a role in neuroplasticity, which affects cognitive flexibility. Zinc supplementation has shown benefit in treatment of AN, with unclear mechanism. This study's primary aim was to investigate correlations amongst mental health, cognitive flexibility, and zinc status, in order to better understand if zinc supplementation benefits in AN are due to metabolic alterations or to mental health changes which impact behaviour. It was hypothesized that that lower zinc status (as measured by the Bryce-Smith zinc taste test (ZTT) and reported symptoms of zinc depletion) would be associated with decreased cognitive flexibility and with increased depressive, anxiety, obsessive-compulsive, and eating disorder symptoms. The secondary aim was to better characterize the ZTT via score comparison with reported seasoning usage and reported zinc depletion symptoms.

Methods: The Perceived Stress Scale, Mental Health Inventory-38 anxiety subscale, Inventory of Depressive Symptoms-SR30, Compulsiveness Inventory, Obsessive Compulsive Inventory-R, Eating Attitudes Test-26, Trail Making Tests A/B, Berg's Card Sorting Test, Haptic Illusion Test, Bryce-Smith ZTT, and a zinc-related factors questionnaire were administered to all participants.

Results: 12 females aged 18-50 were tested and results analyzed using Spearman's and Mann-Whitney U tests. No significant correlations were found between ZTT scores and measures used; however trends in directions that would support the hypothesis were observed.

Conclusion: Due to small sample size and trends observed, it is suggested that the number of participants be increased to better determine potential correlations and that a rough estimate of intake of foods with high zinc levels be introduced for further comparison purposes.

Abstract 13

Transnational farm workers, local health inequities: A role for physicians in supporting migrant farm worker well-being

Anelyse M. Weiler^{1,2}, Michael A. Benusic³, and Yang (Linda) Liu⁴

¹Department of Sociology, University of Toronto; ²Global Labour Research Centre, York University; ³Public Health & Family Medicine, St. Michael's Hospital, University of Toronto, Toronto, Ontario, Canada; ⁴Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

Introduction: Each year, BC employers hire over 6,000 farm workers through the federal Temporary Foreign Worker Program. These migrant farm workers, who are predominantly male and Mexican, often report barriers to accessing health services. This is of particular concern because they work in one of the province's most hazardous industries.

Methods: We conducted a review of the barriers and health concerns of migrant farm workers, gathered through existing literature and original interviews.

Results: Migrant farm workers face barriers to healthcare access due to long working hours, language difference, fear of

deportation, and geographic isolation. Specific health concerns of migrant farm workers include: musculoskeletal issues due to repetitive and stressful ergonomic positions, and dermatological and ocular problems due to exposure to agrochemicals, soil, insects, sun, and climatic extremes. Due to the structure of the migrant farm worker program, physicians could unintentionally have a negative impact on a worker's employment and legal status in Canada, with implications for continuity of health care (e.g. a farm worker is diagnosed with cancer in Canada, a doctor's office phones their employer to seek information about the worker's health coverage and discloses details about the patient's health, the patient is repatriated to Mexico and fails to receive quality health care, and is not "named" to return to the farm in future years).

Conclusion: This information is intended to provide a practical guide to respond to the health needs of this vulnerable population, particularly through translation services, navigating insurance status, and acting with cultural sensitivity. In the process of providing health care, physicians may unintentionally have a negative effect on migrants' employment and legal status. It is therefore imperative for physicians to understand the context under which farm workers are employed in order to ensure they do not exacerbate their precarious working and living conditions.

Abstract 14

Improving primary care access in rural Alberta through a community engagement effort to decrease no shows

Fiona Clarke¹, James Orr², Teresa Ross², and Edward Aasman²

¹Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada; ²Rocky Medical Clinic, Rocky Mountain House, Alberta, Canada

Introduction: Timely access to primary healthcare is an ongoing issue in Canada and internationally, particularly in rural communities where physician supply is limited. In Rocky Mountain House, Alberta, patients' average wait for the third next available appointment is 27 days. The downstream effects of poor access are numerous and include decreased continuity of care, poor patient satisfaction, increased visits to the emergency department, and burnout of physicians. This study aims to engage the community to develop strategies to decrease missed appointments to ultimately improve appointment supply.

Methods: An infographic poster was displayed throughout the clinic to bring awareness regarding the importance of keeping or cancelling all appointments. An anonymous survey was used to gather feedback from patients regarding what changes they feel would help decrease missed appointments. Run charts were used to track weekly no show rates over the course of the study.

Results: There were 34 respondents to the survey, of which 30% had missed a clinic appointment without cancelling. The largest contributing factor was transportation difficulties, followed closely by not being able to get through via phone to cancel, and forgetting about the appointment. Fifty-eight percent of respondents preferred to cancel their appointment via phone, thirty percent via text message, and thirteen percent via e-mail. The majority of respondents thought they would benefit from an automated reminder prior to appointments, a service that is not currently offered. Thus far there has been no change to the weekly no-show rate, which fluctuated around ten percent over the past six months.

Conclusions: In a town with poor access to primary care, patients have identified several areas for improvement with potential to decrease the rate of missed appointments. Future initiatives that should be pursued include addressing barriers to transportation, improving the phone system to facilitate cancellations, and implementing automated appointment reminders.

Abstract 15

Orthostatic hypotension, frailty and falling risk in elderly care home residents

Kimiya Sabbaghan¹, Brett Shaw^{1,2}, Yijian Yang¹, Stephen N. Robinovitch¹, and Victoria E. Claydon¹

¹Department of Biomedical Physiology and Kinesiology, Simon Fraser University, Burnaby, British Columbia, Canada; ²Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

Introduction: Orthostatic hypotension (OH; a significant fall in blood pressure when upright) is a deficit that increases in incidence with age as autonomic dysfunction becomes more common. An accumulation in physiological deficits results in frailty, regarded as a state enhanced vulnerability to adverse outcomes. Here, we quantified a frailty index (FI) and hypothesized that this index would serve as an objective predictor

of OH and falling in a group (n=54) of older adults living in long-term care.

Methods: From the minimum data set document (MDS), a frailty index (FI) was generated from a list of 57 deficits, ranging from 0 (no deficits) to 1.0 (57 deficits). A passive seated orthostatic stress test was used to measure cardiovascular responses to orthostatic stress. Falling rates (falls/year) were extracted from fall incident report forms.

Results: The mean FI was 0.27 ± 0.02 (range 0.07-0.64), and was correlated with age ($r=0.441$; $p<0.001$). Those who were frail ($FI \geq 0.25$) were significantly older, had a larger orthostatic reduction in diastolic arterial pressure ($p=0.05$), along with a poorer ability to recover the upright decline in systolic arterial pressure ($p=0.06$). FI was greater in women (0.31 ± 0.13) than men (0.25 ± 0.12 ; $p=0.07$). OH was present in 47% of subjects. Women were more likely to have OH than men ($p=0.05$). Those who were frail had higher prospective and retrospective rates of falling than the non-frail. Multiple regression analysis predicted prospective falling ($r=0.9$; $p<0.001$) based on FI and whether an individual had a fall in the past year.

Conclusion: The risk of falling in a cohort of elderly long-term care residents can be predicted using a frailty score based on MDS data. Frailty is also related to markers of OH. Risk measurement using this FI offers a potential means to single out individuals for intensive prevention measures in the long-term care setting.

Abstract 16

Historical compliance rates for providing postoperative radiotherapy in oral cavity squamous cell carcinoma

Ashley Hinthner³, Steven C. Nakoneshny^{1,2}, Joseph C. Dort^{1,2,3}, and T. Wayne Matthews^{1,2,3}

¹Cumming School of Medicine, University of Calgary; ²Ohlson Research Initiative, Southern Alberta Cancer Research Institute; ³Division of Otolaryngology - Head and Neck Surgery, Department of Surgery, University of Calgary, Calgary, Alberta, Canada

Introduction: Squamous cell carcinoma of the oral cavity (OSCC) has a 5-year overall survival rate of 50-60%. In 2014 Alberta Health Services released guidelines for treating early and advanced-stage OSCC. Guideline recommendations for

selecting patients that require post-operative radiotherapy (PORT) are dependent on the pathological features of the resected tumour.

Methods: A retrospective analysis was performed to assess the historical selection of OSCC patients requiring PORT in a prospectively collected cohort of patients being treated with primary surgery at the Foothills Medical Centre from January 1, 2009 – December 31, 2013. The primary outcome was compliance with the 2014 AHS guideline recommendations for PORT. The secondary outcome was the selection of PORT according to published pathological indications of high, intermediate and low risk of recurrence. The discordant cases were reviewed to determine the reason for discordance.

Result: Of the 199 patients, there were 32 discordant cases; 2 patients received PORT and 30 patients did not receive PORT contrary to AHS guideline recommendations. There were 24 and 6 patients who did not receive PORT despite high and intermediate risk for recurrence based on the surgical pathology reports, respectively. The reasons for discordance included: clinician decision (n=13), patient refusal (n=6), patient medically unfit/unable to tolerate PORT (n=6), patient lost to follow-up/unknown (n=1), and other (n=4).

Conclusion: Incomplete compliance with the new AHS guidelines and published indications for PORT was observed. Non-compliance was associated with both modifiable and non-modifiable factors. Future work will explore the impact of non-compliance with PORT guidelines on survival and recurrence.

Abstract 17

International surgical outcomes study: A look at local outcomes

Adrianna Woolsey¹, Andrew Suen¹, and Julena Foglia¹

¹Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

Introduction: The International Surgical Outcomes Study (ISOS) was designed to assess multiple outcomes in all types of elective surgery. Several hospitals in Canada have elected to participate, including three centers in Calgary. This presentation will discuss the local outcomes of this observational study.

Methods: The Calgary arm of this cohort study looked at pa-

tients having surgery during the period of May 26 and June 13, 2014. Preoperative, perioperative, and postoperative data were collected from all patients aged 18 years and older undergoing elective surgery at the Foothills Medical Centre (FMC), Peter Lougheed Centre (PLC), or South Health Campus (SHC). All patients spending at least one day in hospital post-operatively were eligible and included in the analysis. Patients were followed for a maximum of 30 days or until discharge from hospital, whichever came earlier.

Results: 281 patients were included; 36 at the SHC, 95 at the PLC, and 150 at the FMC. Of 281 patients, 2 (0.71%) died in hospital within 30 days of their surgery, and 54 (19.2%) patients experienced one or more complications, with 39 (26%) of these patients having had surgery at the FMC, 12 (12.6%) at the PLC, and 3 (8.3%) at the SHC. Complications ranged in severity and included hematoma, ileus, surgical site infection, pneumonia, acute kidney injury, arrhythmia, anemia requiring blood transfusion, anastomotic leak, sepsis, and death, among others.

Conclusion: The 30-day in-hospital mortality rate in Calgary (0.71%) is lower than quoted in recent literature. The overall complication rate of 19.2% reinforces that surgery is not a benign treatment and risks should be thoroughly discussed with all patients beforehand. The FMC had the greatest number of complications, likely due to the fact that cardiac, thoracic, and neurosurgical procedures are performed at that site.

Abstract 18

Effects of after-hours utilization of ultrasound at Foothills Medical Centre

Sundeep Dhaliwal¹, Murad Bandali¹, Alexandra Medellin¹, and Deepak Bhayana¹

¹Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

Introduction: Sonography is a valuable method for imaging the body. It is the preferred imaging modality for many acute presentations in the Emergency Department such as ectopic pregnancy and abdominal pain in young females. An impediment to more widespread use is the limited availability after hours. Just over one year ago, ultrasound has been made available in house, until 2300hrs at the Foothills Medical Centre (FMC). The purpose of this study is twofold. First, to charac-

terize the types of studies being performed after-hours and second, to examine whether increased availability of ultrasound has decreased the number of Computed Tomography (CT) scans after-hours.

Methods: The PACs system was used to determine the number of ultrasound studies completed after hours. After-hours was defined as 1600hrs - 0700hrs. Data was gathered from 8 weeks before and after implementation of after-hours ultrasound. Data on age, gender, study indication, time of study and whether a technician was called back was gathered (technicians called back after 2300hrs). Studies in the Emergency Department as well as relevant studies from Maternity Triage and In-patients were included.

Results: The number of studies pre and post implementation increased from 75 to 389. The portion of callback cases decreased from 58.6% to 8.5%. The number of urgent cases decreased from 41.3% pre to 25.2% post implementation. After implementation a larger variety of studies as well as more in-patients were being scanned. Data on the effect of after-hours ultrasound on the number of CT scans performed is still being collected.

Conclusions: The availability of after-hours ultrasound has resulted in a decrease in the acuity and number of call back cases. Increased availability of ultrasound resulted in more in-patient studies after-hours. Effects on the number of CT scans are still pending.

Abstract 19

Sexually transmitted infections in immigrants and the Canadian Immigration Medical Exam

Mimi Tran¹

¹Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

Background: Nearly 250,000 immigrants enter into Canada each year. Immigrants who were born in countries with higher prevalence of sexually transmitted infections (STI) and who subsequently apply for immigration can impact the epidemiology of infectious diseases in Canada. Moreover, recent immigrants underutilize the healthcare system, attributing to higher health risks. To assess the populations at risk, we conducted a

literature review to examine the current screening requirements for STIs in new immigrants as well as current rates of infection.

Method: A thorough literature review was conducted in PubMed, Medline, and government publications on the current STI screening requirements under the Immigration Medical Exam (IME), current rates of infection among immigrant applicants, and demographics on those infected.

Results: Canadian immigration requires mandatory HIV and syphilis serological screening on all applicants who are ≥ 15 years old. Results summarized below:

HIV - From 2002 to 2003, 634,958 were ≥ 15 years old and were tested for HIV. From this applicant pool, 932 were found to be HIV-antibody-positive (146 per 100,000). Of those who tested positive, 67% were born in Africa and 22% in the Americas. The national rate for HIV in Canada for the 2-year period from 2010 to 2011 is 15.7 per 100,000.

Syphilis - From 2000 to 2004, 2,001,417 were screened for syphilis. From the screening pool, 2,209 applicants were found to be syphilis-positive (110 per 100,000). Of those who tested positive, 54.5% were from Asia and the Pacific region and 16.7% from Africa and the Middle East region. The national rate for infectious syphilis in Canada for the 5-year period from 2007 to 2011 is 23.3 per 100,000.

Conclusion: With the recent cuts to refugee healthcare in Canada, information on the prevalence and demographics of HIV and syphilis immigrants may influence and modify policy and management programs at a regional and national level. In the clinical setting, this information can help practitioners identify at-risk populations and make positive strides to immigrant health outcomes.

Abstract 20

Post dural puncture headaches in the emergency department: a GRADE-based evaluation of the research evidence and recommendations for practice

Michael R. Greene², Andrew Suen², and Eddy Lang^{1,2}

¹Department of Emergency Medicine, ²Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

Introduction: Spinal subdural access is commonly indicated to acquire cerebrospinal fluid (CSF) in provision of diagnostic information, to administer anesthetic agents, or perform specialized imaging studies. Occasionally, inadvertent dural puncture also occurs as a complication of the administration of epidural anesthesia. Resultant decrease in CSF volume may lead to intracranial hypotension and subsequent cerebral vasodilation, with traction of pain sensitive intracranial structures and vessels. The resulting symptom is a headache. These post dural puncture headaches (PDPH) are the most common complication of lumbar punctures, occurring in up to 70% of patients post-LP. At present, no consensus exists for the appropriate treatment of those patients presenting to the emergency department with a PDPH. This study employs the GRADE methodology to evaluate the quality of evidence and develop recommendations for standard treatment practices for those patients with PDPHs presenting to the emergency department.

Methods: The OVID Medline research database was used as the primary source for identifying studies. Secondary searches were conducted on PubMed, EMBASE, and the Cochrane Database of Systematic Reviews. The Guideline Development Tool (GRADE Working Group) was used to create evidence profiles.

Results: A total of 292 papers were identified comparing alternative treatment options for PDPH, from which 31 papers met all inclusion/exclusion criteria. Results indicated a weak to moderate quality body of evidence in support of epidural blood patching, however with potential for significant effect. Weak, low quality evidence for other interventions was also described, including caffeine, gabapentin and triptan class medications.

Conclusion: Post dural puncture headaches of significant severity warrants epidural blood patching (moderate evidence, strong recommendation). Further trials are required to provide sufficient evaluation of the potential benefits and harms of

epidural blood patching and other therapeutic interventions.

Abstract 21

Prenatal programming of mental illness: possible mechanisms and links to poverty

Megan Alton¹

¹Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

Introduction: Maternal adversity experienced during pregnancy is a significant risk factor for poor long-term health outcomes in offspring, including chronic diseases such as diabetes or cardiovascular disease. Recent evidence suggests that this linkage may extend to mental illness. Detrimental prenatal conditions including undernutrition, exposure to alcohol/drugs, or maternal stress are more common in mothers of lower socioeconomic status. This relationship may explain the association of poverty with higher rates of psychopathology.

Methods: A literature review was undertaken examining the association between prenatal adversity and poverty with psychological outcomes. Using the PubMed database, a total of 101 papers were reviewed.

Results: Animal models have found that animals exposed to prenatal stressors are more likely to develop anxious and depressive behaviours, as well as increased behavioural and neurological abnormalities. Human studies have found significant links between in-utero stress and psychopathology; specifically, externalizing disorders, internalizing disorders, schizophrenia, and cognitive defects.

Conclusions: Children of mothers exposed to stress and poverty in pregnancy are at a high risk for developing psychopathology later in life. Mechanisms of this association may be explained by fetal programming, predictive adaptive responses, or epigenetic hypotheses. Interventions to improve prenatal conditions may help to reduce the incidence of future psychopathology.

Abstract 22

A cross-cultural perspective on tuberculosis in Tanzania: Parallels and prophesies. Based on an international medical elective in Tanzania

Nadine Qureshi¹ and Liaquat T. Khan¹

¹Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

Introduction: Tuberculosis continues to be among the major public health concern in Tanzania. The number of tuberculosis cases detected has steadily increased six-fold from 1983 to 2006, due to not only improved screening mechanisms, but also the growing HIV epidemic, urban overcrowding and population growth. The largest cohort of patients is between 15 and 45 years, the same age group affected by HIV/AIDS. Within the past ten years, great steps have been taken to improve the network of TB clinics in Tanzania, with greater access to affordable treatment.

Methods: A review was undertaken to identify the challenges in addressing Tuberculosis in Tanzania, the role of the culture and coexisting epidemics such as HIV/ AIDS, and the effect of the disease burden from social and economic perspectives. Using a predefined search strategy, 43 articles were identified, 19 describing tuberculosis public health interventions in Tanzania. A proposal was constructed to strengthen existing prevention strategies and screening tools.

Results: Tanzania's Ministry of Health and Social Welfare established a strategy for their National Tuberculosis and Leprosy Program that outlines the interventions available to screen, diagnose and treat tuberculosis, with a focus on equity, gender mainstreaming, and accessibility to those most susceptible. Community-based projects in parallel to this framework supplement existing strategies and provide promising models tailored to the needs to particular communities.

Conclusions: The advantages of tailoring Tuberculosis public health interventions to the needs of each community are clear, as are the strategies that are streamlining information and services nationally. Considering that the fastest growing cohort of tuberculosis patients also have HIV/ AIDS, a proposal outlines including specific diagnostic screening protocols in HIV/ AIDS clinics, a model that is in its infancy stages at the PASADA HIV clinic. Future research points to developing

cost-effective analysis to direct the best combination of local measures.

Abstract 23

Systematic review of pediatric Type 1 Diabetes RCTs

Hai Chuan (Carlos) Yu¹, Namrata Hansraj¹, Zafar Hydrie¹, Denise Adams¹, and Sunita Vohra¹

¹CARE Program, Department of Pediatrics, University of Alberta, Edmonton, Alberta, Canada

Introduction: Many pediatric trials are published each year but criticism has been raised regarding the validity of the outcome measures used and the adequacy of reporting of the outcomes, measurement tools and their psychometric properties. Type I diabetes affects many pediatric patients worldwide and many pediatric Type I diabetes randomized controlled trials (RCTs) have been published. However, the extent of reporting problems in this area has not yet been evaluated. We aimed to identify gaps in outcome reporting and heterogeneity of outcomes and outcome measurement tools in pediatric Type I diabetes RCTs and to develop a database of outcome measures for diabetes researchers.

Methods: We searched Medline, Embase, CINAHL, Cochrane Central, and Cochrane SR for pediatric Type I diabetes RCTs. Two independent reviewers screened and extracted data on identified references. Variables extracted included: journal, sample size, participant age, type of study, intervention, control, and details of primary outcome and outcome measurement tools.

Results: While searches identified 8350 unique references, only 164 papers were included. Participant age ranged from 1-20 years. Of the included trials, 32% were of insulin-based interventions, 10% of diet-based treatments, 18% of education-based interventions. Approximately one third of trials did not identify a primary outcome. Of those that did, 62 trials (38%) reported at least one primary outcome and of these, 76% described one outcome as primary and 24% identified more than one. Of the 164 included trials, 74 (46%) failed to address safety or harms of their intervention of interest.

Conclusions: This project has identified gaps in the quality of outcome reporting in pediatric Type I diabetes trials published

over the past 10 years, leading to recommendations for improvements in reporting standards.

Abstract 24

Methadone, patient education, and Vancouver's downtown eastside: A patient workbook

Kirsten Marr¹

¹University of British Columbia, Vancouver, British Columbia, Canada

Background: Methadone maintenance treatment (MMT) was introduced almost 40-years ago as a means to treat opioid withdrawal symptoms (Health Canada, 2008). Vancouver's downtown eastside (DTES) neighborhood houses about 40% of all BC's injection drug users and, it is also home to several MMT programs. Patients that are prescribed methadone treatment for opioid dependence have many educational needs related to their treatment. People that reside in the DTES are confronted with many complex issues such as a higher prevalence of mental illness and physical disabilities, increased rates of communicable diseases, increased drug use, poverty, lower levels of education, inadequate housing and food shortages (Poh et al, 2007; Barbolet et al, 2005). The community represents a population that is complex and has multiple barriers, and special consideration should be taken when applying concepts of health care, including patient education.

Conclusion: The purpose of this project was to create a patient workbook for patients in the DTES that gives specific information to what methadone is, its common side effects, and safety measures while taking methadone. The goal was to present the material in a comprehensive and useful format for persons with a range of intellectual ability and cultures, with an interactive component that allows patients on MMT to actively participate in their treatment and health.

Abstract 25

Tuberculous osteomyelitis/arthritis of the first costoclavicular joint and sternum

Prasan Patel¹ and Robin R. Gray²

¹Cumming School of Medicine, University of Calgary; ²Department of Radiology, Foothills Medical Centre, Calgary, Alberta, Canada

Background: The most common pyogenic causes of osteomyelitis are *Staphylococcus aureus* and *Pseudomonas aeruginosa*, whilst *Mycobacterium tuberculosis* (TB) is a rare causative pathogen in healthy individuals in the world. Risk factors for tuberculous sternal osteomyelitis include but are not limited to: being in or from an endemic area, poor access to health care, immune suppression, and nosocomial exposure to TB. Approximately 25 cases of TB sternal osteomyelitis have been reported in all peer-reviewed journals to date. Bone and joint TB infections account for approximately 6-10% of all extrapulmonary TB cases and about 1% of all TB cases in the United States. Sternal TB osteomyelitis accounts for less than 0.3% of all osteomyelitis cases and 1% of all skeletal TB.

Case Presentation: A young Somali immigrant presented with a two-year history of a large, firm, painful right anterolateral chest wall sternal mass. The patient denied any history of trauma or infection at the site and was asymptomatic. A lateral chest radiograph demonstrated a low density mass isolated to the subcutaneous soft tissue overlying the sternum, ribs and clavicle. Computed tomography (CT) with contrast demonstrated a cystic lesion in the right anterolateral chest wall. Enhanced-CT of the chest demonstrated sclerosis and destruction of the rib and costochondral joint/manubrio-sternal joint narrowing. Ultrasound-guided biopsy and aspiration returned 500cc of purulent, cloudy yellow, foul-smelling fluid. Acid-fast bacilli stain and the nucleic acid amplification test (NAAT) identified and confirmed *Mycobacterium tuberculosis*. A diagnosis of tuberculous osteomyelitis/septic arthritis was made and anti-tuberculosis therapy was initiated.

Conclusion: TB infections may cause severe damage, which can be mitigated if detected with appropriate imaging and treated early. Recognizing that tuberculosis affects up to one third of the world's population should compel physicians to consider a diagnosis of TB in patients with aforementioned risk factors.

Abstract 26

Giant arachnoid granulation in a pediatric patient with a history of focal seizures

Anum Tabish¹ and Clara Ortiz²

¹Cumming School of Medicine, University of Calgary; ²Alberta Children's Hospital, Calgary, Alberta, Canada

Background: Arachnoid granulations are growths of arachnoid membrane that project into the dural sinuses. These sinuses are responsible for draining venous blood and cerebrospinal fluid from the subarachnoid space into the internal jugular vein. Although they are normally found as incidental findings measuring a few millimeters in the transverse and posterior superior sagittal sinus, arachnoid granulations may sometimes grow to fill and dilate the sinuses or expand the inner table of the skull. They normally do not cause symptoms from venous hypertension as a result of partial sinus occlusion.

Case presentation: An 8 year-old boy presented with a one year history of focal seizures and secondary generalization. Investigations were performed to rule out other causes of headaches and complications. Electroencephalography was conducted and was normal. Visual field and acuity was unaffected and a fundoscopic examination revealed a sharp optic disc with no arteriovenous nicking. Imaging studies including computed tomography [CT], magnetic resonance imaging [MRI] and magnetic resonance venography [MRV] were performed. Findings demonstrated a giant arachnoid granulation in the posterior third of the superior sagittal sinus.

Conclusion: The seizures were treated prophylactically with medical therapy and the patient responded well.

Abstract 27

EGFR mutation and estrogen receptor positive lung adenocarcinoma in a male to female transgender patient following estrogen therapy: a case report

Vanessa Di Palma¹, Natalia Guggisberg¹, and Gwynn Bebb¹

¹Department of Medical Oncology and Southern Alberta Cancer Research Institute, University of Calgary, Calgary, Alberta, Canada

Background: Epidermal growth factor receptor (EGFR) mutation positive non-small cell lung cancer (NSCLC) is known to

be prevalent in non-smoking women. A significant correlation exists between EGFR mutation and ER expression in patients with lung adenocarcinoma (LA). Studies suggest a relationship between high NSCLC tumour estrogen receptor β (ER β) expression and poor prognosis. Higher ER β expression has been shown in men with NSCLC and has been associated with metastasis in patients with LA and EGFR mutations. Further, targeting of ER and EGFR in vitro and in vivo models of LA demonstrated anti-proliferative effects when receptors were targeted in tandem. This is a case of a male to female transgender patient with an EGFR mutation and ER positive LA who received estrogen therapy for their transition. The standard dose of estrogen for sex reassignment results in circulating levels of estrogen that are greater than 10 times that of a male.

Case Presentation: A previously healthy 50-year-old male to female transgender patient presented to the ER with a seizure. Magnetic resonance imaging (MRI) suggested metastatic brain disease. Computed tomography (CT) showed a large primary tumour with widespread nodules bilaterally. The diagnosis of primary NSCLC was confirmed with bronchoscopy and biopsy. Pathology showed invasive LA. Bone-scan confirmed metastatic disease. Immunohistochemistry indicated the tumour was EGFR mutation positive and sensitive to the EGFR small molecule inhibitor, Gefitinib. The tumour was found to express high levels of the ER. Chemotherapy with Gefitinib was successful in limiting progression of the disease for several months. The patient passed away a year after diagnosis from progressive disease.

Conclusion: There is evidence that ER plays a role in lung cancer onset and that its expression has negative implications for prognosis, especially in EGFR mutant LA. This case highlights the potential cooperative role of ER and EGFR in NSCLC progression.

hemodynamic changes during the peri-induction period. There are no current guidelines for the anesthetic management of HOCM. We present a case of HOCM that was diagnosed following a peri-induction cardiac arrest.

Case Presentation: A 54 year male was brought to the emergency room (ER) of a tertiary hospital by paramedics after striking a car while riding his motorcycle at high speed. The patient was responsive, alert and oriented, and complained of pain in his thoracic spine and difficulty breathing. He was able to respond to commands with his upper limbs. He had normal sensation, but no motor function to his lower limbs. The patient's heart rhythm was atrial flutter at a rate of 160, blood pressure 96/45, respiratory rate 28. Chest xray showed no pneumo/hemothorax or widened mediastinum. Pelvic xray showed an acetabular fracture. Bedside ultrasound identified no significant source of blood loss. The decision was made to secure the airway and obtain a computed tomography (CT) scan. The patient was given rocuronium, propofol and fentanyl, and intubated successfully on the first pass. After initiating ventilations with a transport ventilator the patient deteriorated and had no palpable pulse. The patient received bilateral chest tubes and return of spontaneous circulation was achieved following 2 rounds of cardiopulmonary resuscitation and 1mg epinephrine. CT was obtained, which identified a T9-10 vertebral dislocation, a large heart, and no additional source of bleeding. After admission to ICU the patient deteriorated again, and a TEE demonstrated HOCM, which was determined to be the cause of his arrest.

Conclusion: If there is a known diagnosis of HOCM, measures can be taken to minimize the risks of induction and intubation. These include maintaining adequate preload and afterload, maintaining sinus rhythm, and minimizing increases in sympathetic tone.

Abstract 28

Minimizing the peri-induction risks of hypertrophic obstructive cardiomyopathy: a case report

Thomas Jared McCormick¹

¹Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

Background: Hypertrophic obstructive cardiomyopathy (HOCM) is a cardiac condition that is especially susceptible to

Abstract 29

Arteriovenous malformation of the upper lip: a case report and literature review

Amanda Eslinger² and Frankie O.G. Fraulin^{1,2}

¹Sections of Pediatric Surgery and Plastic Surgery, Department of Surgery, ²Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

Background: Arteriovenous malformations (AVM) are congenital malformations of abnormal connections between arteries and veins. Most occur intracranially. However, the case presented here involves the face. Initially AVMs are asymptomatic, but they progress, causing ischemic pain, ulceration, and bleeding, disfigurement and psychological distress. Ultimately, they must be fully resected to prevent disfigurement, dysfunction and recurrence.

Case Presentation: A 6-year-old girl was referred to the vascular birthmark clinic for an upper lip mass. On examination, the lip appeared swollen and the lesion felt soft and pulsatile. We noted red-purple discoloration of the hard palate and abnormal dentition. Clinically, speech was affected. Imaging showed the AVM to be supplied mainly by the left facial artery. No bony involvement has been shown but the maxillary bone is thinned. The location of the lesion is a challenging area to resect an AVM and perform a reconstruction, as it is a crucial subunit of the face both in terms of functionality and aesthetics. Consequently a literature review was performed to determine current standard of care for lip AVM.

Literature Review: Eighteen articles were found of which a majority were case reports. The review determined current standard of care for lip AVM was embolization with surgical resection 24-72 hours post-embolization. The majority of articles mentioned the key role of a multi-disciplinary team and the value of pre-intervention diagnostic imaging. Knowledge of the anatomy of the lesion was of utmost importance in embolization and excision.

Conclusion: Following extensive pre-operative imaging and consultation with two pediatric plastic surgeons and an interventional radiologist at the Alberta Children's Hospital and an external consultation with the Boston Children's Group we plan for the patient to undergo embolization of the main AVM feeding vessels, followed by resection 24-48hrs later through an inner lip mucosal approach with no removal of palate, teeth or

skin of the upper lip.

Abstract 30

Exploring linkages of access to drinking water, sanitation and mortality in children under 5 years old in Africa

Victoria David¹

¹Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

Introduction: Access to water and sanitation are paramount to health: research has shown that inadequate water supply, sanitation and hygiene was the second leading cause of disease following malnutrition. This research aims to quantify the linkages between water and sanitation and its impact on child mortality.

Methods: Data, collected through the United Nations database, was captured for % population with access to clean drinking water, % population with access to improved sanitation and child mortality under five. Data was captured for countries in Africa from 1990 to 2012. Linear regression analysis was conducted in Prism.

Results: Initial analysis shows a trend between improved access to water and decreasing child mortality ($R^2=0.51$, $p<0.0001$), improved access to sanitation and decreasing child mortality ($R^2=0.40$, $p<0.0001$) and improved access to both water & sanitation and decreasing child mortality ($R^2=0.55$, $p<0.0001$). Between 1990 and 2012, Malawi had the biggest increase in % access to water (43% absolute increase). During this time period, child mortality dropped by 174.8 deaths per 1,000 live births. Rwanda had the highest increase in access to improved sanitation (34% absolute increase), and also showed a decrease in child mortality of 96.9 deaths per 1,000 live births.

Conclusion: Diarrheal disease incidence would be a better indicator but data was currently unavailable. Mortality was used as a marker since diarrheal disease is one of the leading causes of death in post-neonatal children. While these results appear to show a correlation between water, sanitation & child mortality, the issue is multifactorial and other variables are linked to mortality and may be exacerbated by lack of access to water and sanitation. Further multivariate analysis would be

ideal to discern these relationships as well as efforts should focus on collecting data on diarrheal disease incidence and mortality.

Abstract 31

A global health radio show as a novel method of participatory group reflection on an international medical elective: Insights from the University of Calgary Global Health Concentration

Sarah Elliot¹, Farah Ladak¹, Kate Maki¹, Claire O'Brien¹, Sara Porisky¹, and Rebecca Psutka¹

¹Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

Introduction: The increasing interest in global health has prompted a number of medical schools to develop and diversify opportunities for international exposure. There is better awareness of the ethical implications of medical students completing clinical training abroad. Consequently, it becomes more important that medical students can reflect appropriately on their participation in clinical electives.

Methods: The authors formed the current cohort of GHC students and completed electives in internal medicine and primary care in Tanzania in July 2014. We developed a novel method of reflecting upon our experiences. First, ethical issues were discussed in site-specific groups and then brought to the larger group at daily meetings. Next, we developed questions in key areas including health equity, contribution to medical care, reciprocity, and ethical medical practice. These questions were refined and researched amongst the student group. Then, we identified Tanzanian and Canadian preceptor mentors and sought consent to record structured interviews on our topics of interest to create a two-part radio show. The show aired on CKUT 90.3FM in Montreal on August 12, and August 19, 2014, and ongoing feedback continues via an associated blog.

Results: We utilized a group participatory and goal-oriented approach to unpack the ethical issues that arose with the participation of our local and international mentors. The collaborative discussions were pivotal in contextualizing the insights gained and fostered a unified approach to effect change in this setting. Additionally, interviewing local physicians allowed the GHC to improve relationships with these partners..

Conclusion: We recommend that medical students be guided to complete frequent and ongoing participatory group reflections in addition to individual introspective reflections. Key components of successful participatory group reflection include: i) site-specific group debriefs; ii) whole group debriefs; iii) development of key areas of concern or potential learning; iv) group research on these issues; v) development of structured questionnaires; vi) engagement with local and international mentors; and, vii) producing a tangible reflective outcome such as a documentary, audio, or written piece centered around the key themes identified and previously researched as a group.

Abstract 32

"There is a lot of embarrassment": Reflections of students and educators on sex education in West Bengal, India

Amrita Roy¹ and Rupayan Roy²

¹Department of Community Health Sciences, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada; ²Department of English Language and Literature, Queen's University, Kingston, Ontario, Canada

Introduction: Open discussion of sexuality is largely taboo in Indian society. In 2005, in response to the spiraling AIDS epidemic in India, the West Bengal government introduced a sex-education program called Jeebon Shoihi Shikhya (Lifestyle Education) for implementation in secondary schools in the state. This research, conducted in the early stages of the program's implementation, sought educator and student reactions on the design, content, execution and effectiveness of the Lifestyle Education program.

Methods: Personal interviews with 10 educators and one public official, and focus-group interviews with a total of 298 youth, were conducted during July and August 2006 in Kolkata (Calcutta) and the neighbouring Hooghly and Howrah districts of the state of West Bengal. Bilingual (Bengali and English) semi-structured interview guides were designed and pilot-tested before use. Interviews were audio-recorded with permission, transcribed, and coded for a thematic analysis.

Results: Educators described the challenges in implementing the program, including negative reactions of community members, parents and teachers. This widespread opposition led to the dilution of program content; very little information about

sexuality and sexual health was ultimately conveyed to youth. Students expressed considerable dissatisfaction with the program. They were particularly frustrated at teachers' palpable discomfort, which in turn caused students to also feel embarrassed. Students also expressed disappointment with the minimal information provided, and at the lack of written reference material.

Conclusion: Properly-designed and properly-executed sex education programs for youth are an important component in sexual health promotion, and in public health efforts to combat the global AIDS epidemic. In the years since the conduction of this research, intense debates have raged in West Bengal over the Lifestyle Education program; youth voices have been largely excluded in such discussions. This research suggests that youth strongly desire objective information and accessible resources, delivered without stigma, judgment or embarrassment.

Abstract 33

Prevalence of Chronic Mountain Sickness in India

Bhavdeep S. Rehal^{1,2}, Nidhi S. Panwar¹, and Inderjeet S. Saha^{1,2}

¹A Thousand Metres Above Foundation; ²University of Calgary, Calgary, Alberta, Canada

Introduction: Chronic Mountain Sickness (CMS) is a maladaptation condition that can affect people who reside permanently at high altitude (HA). It is characterized by polycythemia, hypoxemia and dyspnea and can be fatal. Over 140 million people live permanently at HA around the world. Unfortunately, research into CMS is lacking and accurate data on prevalence of this condition do not exist for many regions around the world. In this study we sought to examine prevalence of CMS in the Indian Himalayas.

Methods: We surveyed 83 individuals (69 males) in eight towns across the HA districts of Sirmaur, Kinnaur and Lahaul and Spiti in Himachal Pradesh, India. Altitudes ranged from 2350m to 4150m. We used an adapted Qinghai CMS Scoring System to diagnose CMS. Information related to subject demographics, medical history, socioeconomic status and geography were collected to identify risk factors for CMS. Physiologic recordings of SpO₂ and pulse rate were made via pulse oximetry.

Results: Overall CMS prevalence was 6.17% and mean altitude was 3281m. At altitudes above 3000m, CMS prevalence rose to 13.73%. All cases of CMS were mild and there was a significant positive correlation between CMS scores and altitude ($R=0.784$, $p=0.0213$). Mean SpO₂ was $90.7\% \pm 0.4\%$ and mean pulse rate was $80.3\text{bpm} \pm 1.3\text{bpm}$. SpO₂ significantly correlated with altitude ($R=-0.929$, $p<0.001$). In our study age, gender, and tobacco use were not independent risk factors for CMS. Individuals with CMS lived at higher altitudes than their non-CMS counterparts ($3736.00\text{m} \pm 113.30\text{m}$ versus $3279.80\text{m} \pm 69.50\text{m}$, respectively; $p=0.017$).

Conclusion: CMS prevalence in HA towns of the Indian Himalayas of Himachal Pradesh is 6.17% and 13.73% for towns above 3000m. Further research is required to determine prevalence of CMS in other regions of the world and to determine risk factors associated with CMS.

Abstract 34

Global trends in the rate of cleft lip and palate: bridging the gap

Valerie Bloomfield¹, Chiu-Hsiang Liao¹, and Carrie Howard¹

¹Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

Introduction: Orofacial clefts are the most common craniofacial malformation of the newborn. Worldwide rates vary based on ethnicity and geography. We aimed to assess trends in the rate of cleft lip and palate (CLP) in a large number of countries across several world regions.

Methods: Preferred sources for data collection included national registries, regional registries, health ministries, and academic centers. When available, we captured the number of infants born with (1) cleft lip with or without palate (CL±P), and (2) isolated cleft palate (CP) from 1990 to 2013. Annual rates per 10,000 live births were calculated and countries were grouped according to World Health Organization (WHO) regions (Americas, Europe, South East Asia, Western Pacific, Africa and Eastern Mediterranean).

Results: Data was captured from 52 countries. According to most recent data, the highest total rates of CLP were reported in Venezuela (38 cases/10,000 births), Iran (36 cases/10,000 births) and Japan (30 cases/10,000 births). In total, 64% of

infants had CL±P and only eight countries reported a higher proportion of CP compared to CL±P. Preliminary analysis of temporal trends were assessed within WHO regions from 1990 to 2013. The Americas reported significant increases in the rate of CL±P from 10.3 cases/10,000 births to 12.37 cases/10,000 births ($p = 0.01$) and total CLP from 13.5 cases/10,000 births to 15.3 cases/10,000 births ($p = 0.02$). No other WHO region demonstrated a significant change in CLP rate.

Conclusion: The rate of CLP has remained stable throughout much of the world, with an increase noted in the Americas. Analyses are limited by a paucity of data from certain regions (Africa, Eastern Mediterranean and Asia). Future efforts to develop comprehensive registries will allow for a more accurate assessment of the global burden of CLP.

Abstract 35

What factors predict the fertility intentions and unmet need for contraception among young people in Kenya?

Claire O'Brien¹, Kathryn Church², Isolde Birdthistle², and Susanah Mayhew²

¹Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada; ²London School of Hygiene and Tropical Medicine, London, United Kingdom

Introduction: Kenya demonstrates high rates of fertility, teenage pregnancy, unsafe abortion, maternal mortality, and unmet need for contraception. Young people in Kenya demonstrate variable fertility intentions. To improve reproductive and sexual health services and the health outcomes of young people in Kenya, this report identifies the predictors associated with the desire to have children and with unmet need for contraception.

Methods: Kenyan data from the Integra Initiative 2012 household surveys was used. From the surveys, four groups of predictor variables were identified: socio-demographic, socio-economic, cultural/environmental, and individual life events. To assess associations between these predictors, young Kenyans' fertility intentions, and unmet need for contraception, multivariable logistic regression analyses were completed.

Results: Older age and having previous children was associated with higher odds of desiring children in two or more years among males and females. Males with a partner or an income above 1,000 Ksh/month had higher odds of desiring children

within two years, than single males or those with lower income. Males who had experienced forced sex had higher odds of desiring children in two or more years. Females living with at least three people had higher odds of desiring children in two or more years. Older age and larger household sizes were associated with higher odds of unmet need for contraception among sexually active females.

Conclusion: Age, having previous children, and household size were predictive of females' fertility intentions. Age, having previous children, income, and experience of forced sex were predictive of males' fertility intentions. Reproductive and sexual health services should therefore target sub-groups of young people according to these gender-specific factors. Older age and larger household size were associated with unmet need for contraception, indicating contraceptive programs should target these women. Despite further research needed, evidently there are gender-specific and shared factors that predict Kenyan's fertility intentions.

Abstract 36

Postictal phenomena affect a return to normal activity in children with epilepsy

Sarah J. MacEachern^{1,2}, Sabrina D'Alfonso¹, Nancy Thornton², and Jeffrey R. Buchhalter^{1,2}

¹Cumming School of Medicine, University of Calgary; ²Alberta Children's Hospital Research Institute, Alberta Children's Hospital, Calgary, Alberta, Canada

Background: Following a seizure, patients with epilepsy have reported a multitude of symptoms in the postictal period, ranging from headache to psychosis, with varying degrees of frequency, duration, and severity. However, these phenomena have not been well characterized in children, and their impact on patient well-being is not understood. Therefore, the aim of this study is to characterize postictal symptoms in a population of children with epilepsy.

Hypothesis & Methods: We propose that in a subset of epilepsy patients, postictal symptoms will affect their ability to return to normal childhood behavior. To test this hypothesis, we used a questionnaire-based approach to characterize postictal symptoms, including type, frequency, and duration, in a population of children with epilepsy and we evaluated the impact these symptoms had on the ability of these children to

perform their regular activities. Additionally, we sought to identify aggravating and alleviating factors.

Results: Our study aims to include 500 subjects. Data will be presented at the symposium.

Conclusions: With this preliminary study, we hope to further our understanding of symptoms experienced in the postictal period and gain a better understanding of how these symptoms impact the ability of children with epilepsy to perform their regular activities. To the best of our knowledge, this is the first prospective study of this type in the pediatric population.

Abstract 37

Incidence of Clobazam associated behavioural changes in patients with Lennox-Gastaut syndrome: a single center case series

Kimia Ghavami² and Morris Scantlebury^{1,2}

¹Departments of Pediatrics, Clinical Neuroscience & Alberta Children's Hospital Research Institute, ²Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

Introduction: Clobazam, a 1,5-benzodiazepine has been used in Canada for over thirty years to treat multiple seizure types in children. In 2011, Clobazam was approved by the FDA as adjunctive treatment for Lennox-Gastaut syndrome (LGS). LGS is a devastating childhood epilepsy syndrome characterized by the occurrence of multiple types of seizures and cognitive decline. Two randomized, controlled studies and a follow-up open-label study of Clobazam demonstrated impressive efficacy and safety, with behavioural abnormalities occurring in less than 10% of patients. The aim of this study was to investigate the use of Clobazam, and the incidence of behavioural side effects amongst patients with LGS at the Alberta Children's Hospital (ACH).

Methods: Data from all patients identified with LGS in the EEG database at ACH, between March 2000 and April 2012, were retrospectively extracted from medical records. Factors of interest for Clobazam discontinuation included: age, gender, starting dose, maximum dose, number of concomitant antiepileptic drugs, and MRI findings.

Results: 44 patients with LGS were identified and complete charts were available for 29 patients (69%) which comprised the study population. 19 (66%) of these patients were prescribed Clobazam at some point in their care. Of this group, 9 (47%) patients maintained therapy, 4 patients doing so despite negative behavioural changes. Behavioural changes leading to discontinuation occurred in 6 patients (30%). Starting dose was significantly higher in the group which experienced side effects ($p=0.04$) than the group that did not. Also of note, though not significant, was the higher incidence of MRI lesional findings and simultaneous AEDs in the group which experienced behavioural changes.

Conclusion: This study identified the incidence and variables associated with behavioural abnormalities in LGS patients who are treated with Clobazam. The incidences of aggression and hyperactivity in this study are much higher than that previously reported by other studies. Lower starting doses should be considered to avoid behavioural changes.

Abstract 38

Predicting PIK3CA gene mutation based on gene expression in cervical cancer: a model for targeting gene sequencing to high yield samples

Gordon Jewett¹, John B. McIntyre², Darren R. Brenner³, and Corinne M. Doll⁴

¹Department of Medicine, University of Calgary; ²Department of Pathology and Laboratory Medicine, University of Calgary; ³Department of Cancer Epidemiology and Prevention Research, Cancer Control Alberta, Alberta Health Services; ⁴Department of Oncology, University of Calgary, Calgary, Alberta, Canada

Introduction: As novel gene mutations are identified as drivers of cancer using DNA sequencing, existing gene expression data can be repurposed if it can be used to identify those samples that are more likely to contain mutations. Using existing gene expression data to identify samples more likely to yield valuable sequence information can reduce the cost of further genetic analysis. We therefore propose a method for predicting the mutation status of specific genes based on transcriptome-wide gene expression.

Methods: Our training dataset included *PIK3CA* mutation status for 43 patients with locally advanced cervical squamous cell carcinoma (26 wild-type, 17 mutation carriers) along with corresponding Almac Xcel microarray(c) gene expression data. The classification to nearest centroids (ClANC) method was used to rank genes by standard t-statistics and select class specific genes that form a signature used to differentiate those tumors with *PIK3CA* mutations. Error rates were predicted using 5-fold cross-validation. Validation of the method was not possible due to the absence of a test dataset.

Results: 14 specific gene expression probes were identified for each class (mutation carriers and wild-type) from 110,961 probes on Almac Xcel arrays. Error was estimated at 0.29 with 5-fold cross-validation.

Conclusion: Classification to nearest centroids is a promising method for predicting the mutation status of a specific gene based on gene expression microarray data. Predicted error rates may not be sufficiently low but are limited by small sample size. A larger training set may confirm this as a viable method for targeting resources to sequence samples more likely to contain mutations. A second dataset is required to validate the method and more accurately quantify error rates.

Abstract 39

The cartilage boundary lubricating ability of synovial fluid constituents

Miles Hunter¹ and Tannin Schmidt¹

¹Faculty of Kinesiology, University of Calgary, Calgary, Alberta, Canada

Introduction: Articular cartilage is the tissue covering the ends of long bones that promotes the load bearing, wear resistant and low friction properties of a joint. Within the joint capsule, the constituents of synovial fluid adsorbed to the cartilage surface are in part responsible for facilitating the low friction environment and preventing osteoarthritic degradation. Dipalmitoyl phosphatidylcholine (DPPC) and hyaluronan (HA) are synovial fluid constituents that are yet to have their friction reducing properties fully clarified. Thus, the purpose of this study was to determine the *in-vitro* cartilage boundary lubricating properties of DPPC alone and in combination with HA at physiological concentrations.

Methods: Cartilage explants (n=6) were harvested from the patellofemoral groove of bovine stifle joints. Lubricants of interest were saline (control), DPPC, HA and DPPC+HA in a cartilage-on-cartilage friction test to determine static ($\mu_{static, Neq}$) and kinetic ($\langle \mu_{kinetic, Neq} \rangle$) friction coefficients for each. A 2x2 factorial ANOVA was used to determine the effect of lubricant and pre sliding duration on $\mu_{static, Neq}$ and a one-way ANOVA to determine the effect of lubricant on $\langle \mu_{kinetic, Neq} \rangle$ with Tukey post hoc testing.

Results: DPPC alone and HA alone both significantly (p<0.05) reduced friction ($\langle \mu_{kinetic, Neq} \rangle = 0.089$ and 0.068 , respectively) compared to saline ($\langle \mu_{kinetic, Neq} \rangle = 0.156$). DPPC+HA also significantly reduced friction ($\langle \mu_{kinetic, Neq} \rangle = 0.078$) compared to saline, but was not significantly different from DPPC or HA alone.

Conclusions: At physiologic concentrations, both DPPC and HA act as boundary lubricants at opposing articular cartilage surfaces. Their combination, however, does not create a synergistic effect to reduce friction further than either one independently. These results provide insight into the lubrication of articular cartilage by synovial fluid constituents and their potential application to biotherapeutic treatments for osteoarthritis.

Abstract 40

Laquinimod reduces neuronal caspase-6 activation and axonal degeneration in vitro

Dagmar E. Ehrnhoefer¹, Michelle Tsang¹, Xiaofan Qiu¹, and Michael R. Hayden¹

¹Centre for Molecular Medicine and Therapeutics (CMMT), Department of Medical Genetics, CFRI, University of British Columbia, Vancouver, Canada

Background: Laquinimod is an immunomodulatory compound that reduces relapse rate, brain atrophy and disability progression in multiple sclerosis. It has well-documented effects on inflammation, is widely distributed in the CNS and has been shown to ameliorate axonal damage in vitro and in vivo through an unknown mechanism. We have shown recently that caspase-6 is an important mediator in axonal degeneration, since sympathetic neurons derived from caspase-6 $-/-$ mice do not degenerate when cultured in the absence of neuronal growth factor (NGF). We therefore investigated whether

the beneficial effect of Laquinimod on axonal damage is mediated by caspase-6.

Methods: Cell-free and cell-based enzymatic activity assays were used to determine whether Laquinimod directly inhibits caspase-6. To investigate an effect on intraneuronal caspase-6 activity, primary cortical neurons were treated with camptothecin in the presence or absence of Laquinimod, and cleavage of the caspase-6 specific substrate lamin A was quantified by ELISA. Axonal degeneration of primary sympathetic neurons from the superior cervical ganglion (SCG) was induced by NGF withdrawal in the presence or absence of Laquinimod.

Results: Laquinimod did not directly inhibit caspase-6 activity in cell-free or transfection-based cellular systems. However, the presence of Laquinimod in camptothecin-stressed primary cortical neuron cultures led to a significant decrease in caspase-6 activation. In cultures of primary SCG neurons, Laquinimod partially protected axons from degeneration after NGF withdrawal, a process that is specifically dependent on caspase-6 activity, in agreement with the reduction of caspase-6 activity observed in stressed cortical neurons.

Conclusions: The beneficial effects of Laquinimod described so far involve neuroprotection through the downregulation of glial activation, whereas our findings represent a novel, purely neuronal mechanism of action. We propose that by preventing neuronal caspase-6 activation and axonal degeneration, Laquinimod might also provide benefits in other neurodegenerative disorders associated with excessive activation of caspase-6, such as Huntington's disease.

Abstract 41

Circulating tumor cells: potential prognostic and predictive virtual biopsy --enumeration and biomarker analysis of circulating tumor cells

Jinghui Hu¹, Alexander Klimowicz², Brant Pohorelic², Carrie Shemanko³, Patricia Tang¹, and Don Morris¹

¹Department of Oncology, Tom Baker Cancer Centre, Alberta Health Services; ²Department of Oncology, University of Calgary; ³Department of Biological Sciences, University of Calgary, Calgary, Alberta, Canada

Introduction: Circulating tumor cells (CTCs) are tumor cells that are disseminated in the blood. The number of CTCs enu-

merated using CellSearch (Veridex, LLC) has been FDA approved for predicting prognosis of patients with metastatic breast cancer, colorectal cancer, and prostate cancer. CTCs can also be used as a liquid biopsy which can be easily obtained from patients' peripheral blood to evaluate biomarkers.

Methods: We have set up the CellSearch system for enumerating CTCs and developed methods of quantitative protein biomarker analysis on CTCs. Due to the qualitative nature of the CellSearch system for biomarker analysis on CTCs, we developed quantitative biomarker analysis of CTCs using ficoll separation followed by fluorescent immunocytochemistry staining and AQUA analysis.

Results: Since interindividual variability in interpretation of CellSearch results has been previously reported, we completed a concordance study for our CellSearch System and result interpretation with Veridex using control samples. Our local enumeration results are similar to the Veridex results [Tom Baker Cancer Center (22±6) versus Veridex (22±3), n=7]. The CTCs were identified based on cytokeratin positive and CD45 negative staining. Biomarker quantification was performed by AQUA analysis of biomarker signals on the cytokeratin mask and CD45 mask. Using these methods, we have developed three markers for breast cancer CTCs, including Estrogen Receptor, Receptor Activator of Nuclear Factor κ B, and the Prolactin Receptor.

Conclusions: In conclusion, with these valuable platforms of CTC analysis established, we can evaluate novel prognostic and predictive factors for cancer metastasis.

Abstract 42

Obstructive sleep apnea treatment improves arterial stiffness and alters vascular sensitivity to Angiotensin II in humans

David D.M. Nicholl¹, Patrick J. Hanly^{1,2}, Jennifer M. MacRae^{1,3}, George B. Handley², Brenda R. Hemmelgarn^{1,3}, Marc J. Poulin¹, Darlene Y. Sola¹, and Sofia B. Ahmed^{1,3}

¹Department of Medicine, University of Calgary, Calgary, Alberta, Canada; ²Sleep Centre, Foothills Medical Centre, Calgary, Alberta, Canada; ³Alberta Kidney Disease Network

Background: Obstructive sleep apnea (OSA) is a recognized risk factor for the development of vascular disease, particularly

hypertension. Limited studies suggest a prominent role for the renin-angiotensin system (RAS), activation of which is deleterious to kidney and cardiovascular function. We sought to determine the effect of continuous positive airway pressure (CPAP) therapy on arterial stiffness and the RAS at baseline and in response to Angiotensin II (AngII), in humans with OSA.

Methods: Sixteen newly diagnosed (12 men, 4 postmenopausal women; 50 ± 3 y) OSA subjects (respiratory disturbance index [RDI] $> 15 \text{ hr}^{-1}$) with nocturnal hypoxia [oxyhemoglobin saturation $\{\text{SaO}_2\} < 90\%$ for $> 12\%$ of night] who were otherwise healthy were studied pre- and post-CPAP therapy (1 month of adequate therapy $[> 4 \text{ h/night}]$). Subjects were studied in high salt balance, a state of maximal RAS suppression. Arterial stiffness (aortic augmentation index [AIx] and carotid femoral pulse wave velocity [PWV]) was measured by applanation tonometry at baseline and in response to a graded AngII infusion ($3 \text{ ng/kg/min} \cdot 30 \text{ min}$, $6 \text{ ng/kg/min} \cdot 30 \text{ min}$, recovery $\cdot 30 \text{ min}$). The primary outcome was the effect of CPAP treatment on the AIx and PWV responses to AngII at 60 min and the recovery period.

Results: CPAP corrected OSA (RDI: 44 ± 5 vs $4 \pm 1 \text{ hr}^{-1}$, $p = 0.005$; duration $\text{SaO}_2 < 90\%$: 35 ± 5 vs $5 \pm 2\%$ of night, $p = 0.005$) and reduced baseline AIx (20.6 ± 1.7 vs $15.9 \pm 3.1\%$, $p = 0.024$), but did not affect baseline PWV (8.44 ± 0.53 vs $8.29 \pm 0.42 \text{ m/s}$, $p = 0.6$). There was a significant increase in AIx (8.8 ± 1.1 vs $12.7 \pm 2.1\%$, $p = 0.044$) and a non-significant decrease in PWV (1.16 ± 0.37 vs $1.09 \pm 0.39 \text{ m/s}$, $p = 0.6$) sensitivity to AngII (all values pre- vs post-CPAP). There was no change in how quickly AIx returned to baseline after AngII challenge (1.3 ± 1.6 vs $1.3 \pm 2.6\%$, $p = 0.8$), but a more rapid recovery was observed with PWV post-AngII challenge (1.11 ± 0.45 vs $0.41 \pm 0.21 \text{ m/s}$, $p = 0.055$).

Conclusions: Our preliminary observations suggest OSA treatment with CPAP may improve arterial stiffness through changes in vascular sensitivity to AngII.

Abstract 43

Administration of a cannabinoid receptor 1 agonist rescues learning and memory behaviors after a traumatic brain injury in male rats

Marium Arain¹, Maida Khan¹, Laura A. Craig², and Stan T. Nakanishi¹

¹Alberta Children's Hospital Research Institute, University of Calgary; ²Regeneration Unit in Neurobiology Core Facility, University of Calgary, Calgary, Alberta, Canada

Introduction: TBI is one of the major causes of central nervous system dysfunction leading to cognitive impairments. Nearly 1.7 million people in United States suffer from traumatic brain injury (TBI) annually. To date, there is no effective treatment to rescue or recover the learning and memory functions following a TBI. Previous studies have elucidated several pathological consequences of TBI which include excitotoxicity, neuroinflammation, and disrupted metabolic functions. The cannabinoid receptor 1 (CB1R) is a G-protein coupled receptor that can reduce excitotoxicity and neuroinflammation, and can modulate mitochondrial functions.

Methods: We tested the hypothesis that administration of a CB1R agonist (arachidonyl-2'-chloroethylamide, ACEA) after a TBI would rescue learning and memory-linked behaviors. To test this hypothesis, we randomly assigned young adult male Sprague-Dawley rats ($n = 33$) into five groups i.e. TBI + drug ($n = 8$), TBI + vehicle ($n = 8$), sham + drug ($n = 6$), sham + vehicle ($n = 7$), or naïve ($n = 4$). All the groups were subjected to either a controlled cortical impact (CCI) injury or sham injury followed by the administration of ACEA (1 mg/kg) or vehicle daily for one week. We conducted Morris water maze (MWM) and novel object recognition task (NOR) to determine the post injury memory retention.

Results: The results showed that CCI-injured (TBI + vehicle) rats exhibit significant deficits in the memory-associated Novel Object Recognition and Morris Water Task tests. In contrast, the CCI-injured rats that received the ACEA treatment showed no deficits in their ability to do these tests, and their behaviors were indistinguishable from naïve animals despite an obvious brain lesion.

Conclusion: The results presented here suggest that cannabinoid agonist treatment could potentially be beneficial for the treatment of traumatic brain injuries. However, future studies

should focus more on the risks of a cannabinoid treatment plan and its implications to justify its use in patient population.

Abstract 44

Vaccinia virus B4R-null mutants exhibit decreased virus spread

Kristin Burles¹, Chad R. Irwin¹, Robyn-Lee Burton¹, Jill Schreiwier², David H. Evans¹, R. Mark Buller², and Michele Barry¹

¹Li Ka Shing Institute of Virology, Department of Medical Microbiology and Immunology, University of Alberta, Edmonton, Alberta, Canada; ²Department of Molecular Microbiology and Immunology, Saint Louis University School of Medicine, St. Louis, Missouri, USA

Introduction: The *Poxviridae* is a large family of viruses whose members infect a wide variety of hosts. The most well-known member, variola virus, is the causative agent of smallpox, a disease that killed more humans in recorded history than all other infectious diseases combined. Though smallpox was eradicated in 1977, other poxviruses cause clinically relevant infections, and recent outbreaks of monkeypox underline the importance of studying these viruses. Vaccinia virus (VACV), the prototypic poxvirus, produces two types of infectious virions: mature virions and extracellular virions. Extracellular virions undergo additional membrane-wrapping steps compared to mature virions, and remain associated with the cell until they stimulate actin rearrangement. This work characterized the role of the VACV ankyrin/F-box protein B4R in virion morphogenesis, release, and spread.

Methods: Recombinant viruses devoid of B4R were generated and compared to parental viruses using the functional assays described below.

Results: Viruses devoid of B4R had a reduced plaque size in tissue culture, and decreased ability to spread, as assessed by multiple step growth analysis. Electron microscopy indicated that B4R-null viruses still formed mature and extracellular virions; however, there was a decrease of virions released into the media following deletion of B4R. Notably, confocal microscopy revealed that deletion of B4R did not affect the ability of the virus to rearrange actin; however, the VACV large deletion mutant, VACV811, which is missing 55 open reading frames, had decreased ability to produce actin projectiles, suggesting

that additional mediators of actin rearrangement exist in VACV. Using an *in vivo* mouse model, we demonstrate that ectromelia virus devoid of EVM154, the homologue of B4R, was unable to spread to organs following infection of C57BL/6 mice.

Conclusion: Our results indicate that B4R is a mediator of virus spread, and suggest that additional unidentified mediators also exist in VACV.

Abstract 45

Determining the downstream signaling pathways involved in the prostaglandin E2-mediated repression of inflammatory mediator output in human myometrial cells

Hayley S. Levinson¹, Andrea A. Mosher¹, Stephen Wood², and Donna M. Slater^{1,2}

¹Department of Physiology & Pharmacology, University of Calgary; ²Department of Obstetrics & Gynecology, University of Calgary, Calgary, Alberta, Canada

Introduction: While prostaglandin production is increased in human labour, the precise role remains unclear. Our group has previously shown that prostaglandin E₂ (PGE₂) inhibits spontaneous myometrial contractions and represses interleukin-1 β (IL-1 β)-induced inflammatory mediator output by human myometrial cells. The biological effects of PGE₂ occur via activation of the G protein coupled receptors EP₁-EP₄. The EP₁ and EP₃ subtypes are coupled to G α_q and G α_i with stimulation leading to increased intracellular calcium levels or inhibition of cAMP production, respectively. In contrast, both EP₂ and EP₄ couple to G α_s and stimulation leads to increased cAMP production. Subsequently, cAMP may activate multiple pathways, including protein kinase A (PKA) and/or exchange proteins directly activated by cAMP (Epacs). The objective of this study is to determine the downstream signaling pathways involved in the PGE₂-mediated repression of inflammatory mediator output.

Methods: Lower segment myometrial biopsies were collected from term elective Caesarean deliveries prior to labour onset and used to isolate myometrial cells (n=5, 37-40 weeks gestation). Cultured myometrial cells were treated with IL-1 β in the presence of PGE₂, specific EP agonists or PGE₂ +/- cAMP

analogues selective for PKA or Epacs. Inflammatory mediator output (CXCL8, CCL2, CSF2) was measured by ELISA.

Results: IL-1 β increased CXCL8, CCL2, and CSF2 output by cultured human myometrial cells ($p < 0.001$). This effect was repressed by pre-treatment with PGE₂, an EP₂ selective agonist, an EP₄ selective agonist, and PKA-selective cAMP analogues ($p < 0.05$), but not Epac-selective cAMP analogues.

Conclusion: The PGE₂-mediated repression of IL-1 β -induced inflammatory mediator output in human myometrial cells occurs through activation of the EP₂ and EP₄ receptor subtypes, but not EP₁ or EP₃. Based on the use of selective pharmacological agents, the downstream signaling pathways involved in this effect are likely mediated by PKA, but not Epacs.

Abstract 46

Giardia duodenalis cysteine-like cathepsin proteases disrupt and cleave a key homeostatic cytoskeletal protein, villin

Amol Bhargava^{1,2,4}, James A. Cotton^{1,2,4}, Robin M. Yates³, and Andre G. Buret^{1,2,4}

¹Department of Biological Sciences, ²Inflammation Research Network, ³Comparative Biology and Experimental Medicine, ⁴NSERC CREATE Host-Parasite Interactions, University of Calgary, Calgary, Alberta, Canada

Introduction: Disruptions of intestinal epithelial barrier and epithelial maintenance are implicated in the pathophysiology of a variety of intestinal disorders. *Giardia duodenalis*, a non-invasive protozoan parasite of the upper small intestine, closely associates with intestinal epithelial cells to induce pathophysiological effects resembling chronic inflammatory GI diseases, including intestinal epithelial barrier dysfunction via mechanisms that remain obscure. The *Giardia* genome contains genes for cathepsin B-, C-, and K/L-like cysteine proteases; however, their roles are largely unknown. The aims of this study were to characterize *Giardia* cathepsin activity as they infect human intestinal epithelial cells, and characterize their pathophysiological effects, particularly on cytoskeletal and tight junctional proteins.

Methods: *G. duodenalis* trophozoites (Assemblage A isolates NF, S2 or Assemblage B isolate GS/M) were co-incubated *in vitro* with human colonic monolayers (Caco-2) for 2 or 24

hours. *Giardia* trophozoite lysates, supernatants, and host cell monolayers lysates were isolated and incubated with cathepsin fluorogenic substrates to measure cathepsin activity. *Giardia* trophozoites pretreated with a broad spectrum cysteine protease inhibitor (E64d) were co-incubated with Caco-2 monolayers. Co-incubation of *Giardia* trophozoites with Caco-2 cells was also done in the presence of an MLCK inhibitor, ML-9. Caco-2 lysates were also incubated with *Giardia* trophozoite lysates in the presence of E64d. Host cell lysates were processed for Western blotting to assess effects of *Giardia* cathepsins on tight junctional integrity (ZO-1) or cytoskeletal proteins (Villin).

Results: *Giardia* trophozoites express intra-trophozoite as well as secretory/excretory cathepsin activity, in the presence or absence of Caco-2 monolayers, and in an assemblage-independent manner. No changes in cathepsin activity within host cells were detected in the presence of *Giardia* from either assemblage. Pretreatment of *Giardia* NF trophozoites with E64d inhibited *Giardia* cathepsin activity, but failed to block *Giardia*-induced ZO-1. However, pretreatment of *Giardia* trophozoites with E64d prevented the breakdown of villin, a key actin-bundling protein that is responsible for the homeostatic maintenance of epithelial microvilli. Co-incubation of Caco-2 and *Giardia* NF trophozoite lysates with E64d prevented villin breakdown. In addition, ML-9 prevented *Giardia*-induced cleavage of villin after 24 hours but not 2 hours of incubation.

Conclusion: *Giardia* trophozoites express and release cathepsin-like cysteine proteases. *Giardia*-induced villin, but not ZO-1, breakdown is mediated in part by cathepsin-like proteases, which may later be propagated by an MLCK-dependent pathway. This suggests that *Giardia* cathepsins at least in part contribute to this parasite's pathogenesis through a disruption of cytoskeletal proteins.

Abstract 47

Comprehensively evaluating stakeholder experiences during the implementation of a single-entry model for elective surgery in Winnipeg: a multi-stakeholder national project under the CIHR Evidence-Informed Healthcare Renewal (EIHR) Roadmap Signature Initiative

Zaheed Damani¹, Eric Bohm², Gail MacKean¹, Brie DeMone³, Brock Wright⁴, Tom Noseworthy¹, and Deborah Marshall¹

¹Department of Community Health Sciences, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada; ²Department of Surgery, University of Manitoba; ³Manitoba Health, Healthy Living and Seniors; ⁴Winnipeg Regional Health Authority, Winnipeg, Manitoba, Canada

Introduction: With single-entry models (SEMs) for elective surgery, referrals are pooled, assessed and patients can see the next-available surgeon through a central intake process. The Winnipeg Central Intake Service (WCIS) is a SEM to manage patients awaiting hip or knee replacement surgery. We will elucidate the development, implementation and impact of the WCIS on health/health services. We used a pre/post mixed-methods case study approach to measure impact on six dimensions of quality: acceptability, accessibility, appropriateness, effectiveness, efficiency and safety.

Methods: Assessment of experiences, changes in viewpoints and acceptability towards SEMs were elicited using semi-structured interviews with patients, family physicians, orthopaedic surgeons, surgical office assistants and WCIS team members (policy-makers, managers and planner). Anticipated/unanticipated, desirable/undesirable implications of the WCIS were assessed at macro (provincial), meso (regional), micro (clinical/patient) levels.

Results: Seventy pre-implementation stakeholder interviews are complete: expectations have been divergent and acceptance of SEMs has been conditional not universal. Policy-makers and patients favour the WCIS for reduced wait times and better availability of patient care information (appointment dates, preparation for surgery etc.). Family physicians and surgeons appreciate the streamlined referrals but are concerned about loss of autonomy and potential to permanently improve access. While initially opposed due to increased workload, surgical office assistants remain optimistic as they work with the WCIS team to adapt to and simplify processes. Greater assessment of

capacity and readiness for change would have improved initial uptake/awareness among stakeholders. Continual improvement based on stakeholder feedback will be critical for sustained success through better identification, assessment, response to patient and system needs.

Conclusion: Through collaboration with national partners/knowledge-users including Winnipeg Regional Health Authority and Manitoba Health, findings will be translated into policy and practice to improve the WCIS, patient experience and system performance while strengthening other existing SEMs and informing the design and implementation of future SEMs across practice areas and Canadian jurisdictions.

Abstract 48

Susceptibility weighted imaging detects early venous deoxyhemoglobin changes in a model of multiple sclerosis

Nabeela Nathoo^{1,2}, Ying Wu¹, James A. Rogers^{2,3}, V. Wee Yong^{2,3}, and Jeff F. Dunn¹⁻⁴

¹Department of Radiology, ²Hotchkiss Brain Institute, ³Department of Clinical Neurosciences, ⁴Experimental Imaging Centre, University of Calgary, Calgary, Alberta, Canada

Introduction: Susceptibility weighted imaging (SWI) is a magnetic resonance imaging (MRI) method sensitive to deoxyhemoglobin. SWI has shown altered deoxyhemoglobin content in the venous vasculature of multiple sclerosis (MS) patients. Previously, using SWI, we had shown elevated deoxyhemoglobin content in mice with experimental autoimmune encephalomyelitis (EAE) during peak disease. Here, the aim was to investigate changes to deoxyhemoglobin content of the venous vasculature over time in the EAE model using serial in vivo SWI.

Methods: Mice induced with EAE ($n=9$) were imaged at 9.4T with 3D gradient echo with flow compensation for SWI at four time points: baseline, day 7 (pre-motor dysfunction), day 12 (onset of motor dysfunction) and day 16-18 (peak disease). Naïve control mice ($n=3$) were matched with EAE for imaging time points.

Results: Hypointensities (dark spots) on SWI, corresponding to changes in venous deoxyhemoglobin content, were observed at day 7 in EAE mice, before motor dysfunction was present.

The number of SWI hypointensities did not change substantially amongst naïve controls over the imaging time points, but there was great heterogeneity amongst EAE mice over the disease course. In all EAE mice, the number of SWI hypointensities was at a maximum either before or at the same time as maximum motor dysfunction (maximum EAE clinical score), but never after.

Conclusion: These data support the theory that increased oxygen extraction fraction and hypoxia may take place early in the EAE disease course, which can be detected with SWI. The cause and significance of these alterations in venous deoxyhemoglobin content require further investigation.

Abstract 49

Wild Wellness: A review of the health implications of play in natural spaces on childhood development and well-being

Ian MacNairn^{1,2}

¹Department of Anthropology, and ²Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

Introduction: The last thirty years has seen increased attention on inquiry into the role of play and activity in green, natural spaces and its relation to childhood health and development. Previous studies have focused on a variety of topics including physical, mental, emotional and social health outcomes in children and adults. Here, I hypothesize that time spent in play and activity in natural spaces during childhood correlates with myriad positive health outcomes both in childhood.

Methods: This paper is a meta-analysis of existing literature and research that has examined the role of activity in natural spaces with concurrent and subsequent implications for individual and population-level health outcomes. Focus is placed on changes that activity in natural spaces, when compared with inactivity as well as activity in human-created spaces, have on physical, mental, emotional (individual-level) and social (population-level) outcomes for children's health. The paper concludes with an overview of public and private initiatives focused on encouraging activity in natural spaces implemented in Canada along with corresponding preliminary results in terms of participation and health outcomes.

Results and Conclusions: Cumulative insights shared in the field suggest that increased time spent in play and activity in natural spaces results in lowered morbidity both during childhood as well as in later adolescence and adulthood. The myriad positive health changes include reduced symptoms of attention deficit disorder (ADD), decreased reliance on antidepressant prescription medication, reduced stress and anxiety, reduced rates of obesity and high blood pressure, increased concentration and creativity, and improved self-esteem and body-image. Additionally, children who spend time playing in outdoor, natural spaces have improved interpersonal communication as well as improved social interaction and social cohesion during childhood and adulthood.

Abstract 50

Harmless commensal microbial neighbors synergistically trigger *Pseudomonas aeruginosa* virulence genes in Cystic Fibrosis

Christina S. Thornton¹, Matthew L. Workentine⁴, Christopher D. Sibley¹, Harvey R. Rabin^{1,2}, Douglas G. Storey³, and Michael G. Surette^{1,4}

¹Department of Microbiology, Immunology and Infectious Diseases, ²Adult Cystic Fibrosis Clinic, ³Department of Biological Sciences, University of Calgary, Calgary, Alberta, Canada; ⁴Departments of Medicine and Biochemistry and Biomedical Sciences, McMaster University, Hamilton, Ontario, Canada

Introduction: Cystic fibrosis (CF) is the most common lethal genetic disease among Caucasians. 90% of CF patients succumb to pulmonary failure from chronic respiratory infections. Traditionally, research has focused on a narrow spectrum of microorganisms as principal pathogens such as *Pseudomonas aeruginosa* (PA). The oropharyngeal flora (OF) have been implicated in enhancing pathogenesis of PA while acting as benign commensals, otherwise known as "synergens". These interactions may skew the balance between clinical stability and acute pulmonary exacerbation, leading to hospitalization. The objectives here were to evaluate these interactions and construct synergen mutants to identify the pathway(s) involved.

Methods: Seven oropharyngeal-derived microbes were isolated from sputum of adult CF patients (*Streptococcus* sp, *Rothia* sp and *Actinomyces* sp) and screened *in vitro* for affecting PA virulence gene expression in co-cultures. The ability of these 'be-

nign' microbe 'synergens' to stimulate PA virulence genes was evaluated using transformed PA reporters harboring luciferase constructs for known virulence gene promoters. The luciferase light production caused by the co-culture vs. monoculture of PA was monitored to quantify 'synergen' activity by measuring changes in light production. Transposon libraries in the synergens were constructed with 8000 mutants screened.

Results: Up-regulation of PA virulence gene expression was seen for all 7 synergens tested. The virulence pathways affected were for quorum sensing or bacterial communication. The highest up-regulation was by *Streptococcus*. sp, with 1800-fold increased virulence gene expression in co-culture as compared to PA alone. From 8000 synergen mutants, 526 were isolated as hits involved in co-culture. 61 of these mutants were conserved in all PA reporters, suggesting common interaction pathway(s) triggered by the synergens. 35 mutants displayed 10-fold or greater activation in co-culture as compared to the wild-type, demonstrating a gain-of-function mutation.

Conclusion: We have found that seemingly harmless non-pathogenic oropharyngeal 'synergen' microbes can trigger virulence genes in PA found in CF patients. The production of secondary signaling molecules have been shown to influence pathogen virulence profiles by modulating bacterial cell-cell communication pathways. Understanding the way in which commensal microbes synergistically trigger virulence will lead to better treatment and management of CF.

Abstract 51

Human macrophages provide a replication niche for *B. cenocepacia* to escape neutrophil killing and enhance bacterial replication

Allison McDonald¹ and David P. Speert¹

¹Centre for Understanding and Preventing Infection in Children, Department of Microbiology and Immunology, University of British Columbia, Vancouver, British Columbia, Canada

Introduction: Pulmonary innate immunity protects against inhaled pathogens through a combination of defenses that include tissue-resident macrophages and recruited neutrophils. *B. cenocepacia* is an opportunistic pathogen that causes severe respiratory infections in immunocompromised individuals, particularly those with cystic fibrosis or chronic granulomatous

disease. Infections are characterized by neutrophil infiltration and excessive inflammation. The ability of the bacteria to survive and replicate within macrophages may contribute to their ability to evade host inflammatory response and cause chronic infections.

Methods: The collaborative effects of human macrophages and neutrophils in controlling survival of *B. cenocepacia* were investigated by co-culture experiments. The number of bacterial colony-forming units was measured in cultures with and without macrophages and/or neutrophils over time. The profiles of inflammatory mediators produced from co-culture experiments were also examined.

Results: While neutrophils were more efficient than macrophages in phagocytosing *B. cenocepacia*, the bacteria were able to quickly replicate within primary monocyte-derived macrophages, which offered a large survival advantage compared to bacterial growth in media alone. Proliferation required entry into macrophages and neither macrophage-released factors nor macrophage lysates were capable of enhancing bacterial growth. Only when neutrophils were co-cultured in great excess of macrophages were they able to control the growth of *B. cenocepacia* and to dampen the release of inflammatory mediators from macrophages.

Conclusion: This study suggests that macrophages have a dominant effect over neutrophils in the ability to affect *B. cenocepacia* growth and that an excess of neutrophils is required to abrogate this effect. These observations are consistent with the massive infiltration of neutrophils during respiratory infection with *B. cenocepacia* and may explain the skewing of host defense toward neutrophilia in an attempt of the host to control infection.

Abstract 52

The presence of a TRP-NCX signaling complex in the regulation of endothelial function

Chiu-Hsiang Liao¹, Emma Walsh¹, Serena Hou¹, Casey van Breemen¹, Andy Braun¹, and William Cole¹

¹Department of Physiology and Pharmacology, University of Calgary, Calgary, Alberta, Canada

Introduction: Appropriate release of nitric oxide (NO) is critical for normal physiological functioning of the cardiovas-

cular system. Although changes in intracellular Ca^{2+} concentration ($[\text{Ca}^{2+}]_i$) in endothelial cells (ECs) is thought to play an important role in the coordination of NO release, the molecular mechanism underlying this influx is poorly understood. Sustained Ca^{2+} influx in ECs has been widely assumed to be due to the presence of transient receptor potential (TRP) protein-containing non-selective cation channels (NSCC) in the PM. However, the non-selective nature of TRP channels for cations indicates that TRP channels can also act as a Na^+ entry pathway. Na^+ accumulation under the plasma membrane could then facilitate sodium-calcium exchanger (NCX) activity in the reverse, Ca^{2+} entry mode. The role of NCX as a Ca^{2+} entry pathway has yet been studied in detail in ECs.

Methods: Intracellular Ca^{2+} measurements were made with FURA-2AM fluorometry. The effect of luminal flow on arterial diameter was studied using pressurized myography in endothelium-intact rat cerebral arteries (RCAs). Co-localization of proteins was assessed using proximity ligation assay (PLA). A three-step method of western blotting was utilized to detect eNOS phosphorylation at Ser1177.

Results: We identified the presence of a signaling complex comprised of stromal interaction molecule 1 (STIM1), transient receptor potential protein (canonical subtype) 1 (TRPC1), and the $\text{Na}^+/\text{Ca}^{2+}$ exchanger 1 (NCX1) in cultured ECs. Inhibition of NCX by KB-R7943 significantly impaired agonist-induced phosphorylation of endothelial NO synthase (eNOS) at serine 1177 (S1177-eNOS). Recruitment of the NCX in reverse mode was also shown to play an important role in flow-mediated dilation (FMD) and the corresponding phosphorylation S1177-eNOS.

Conclusions: Our findings suggest that a TRP-NCX signaling complex mediates Ca^{2+} influx leading to a rise in $[\text{Ca}^{2+}]_i$, NOS activation and NO release to evoke FMD in cerebral artery.

Abstract 53

Rapid degradation of the macrophage cytoskeleton upon contact with the gastrointestinal parasite *Entamoeba histolytica*

Joelle St-Pierre², France Moreau¹, and Kris Chadee¹

¹Department of Microbiology, Immunology and Infectious Diseases, ²Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

Introduction: *Entamoeba histolytica* (*Eh*) is the causative agent of amebiasis, a disease responsible for ~100 000 deaths/year. In most cases, *Eh* colonizes the mucus layer of the colon without causing symptoms, however in some individuals *Eh* invades the colonic mucosa causing amebic colitis. The first response of the host at sites of *Eh* invasion is a robust acute inflammatory response mediated by macrophages. *Eh*-macrophage interaction is thus a critical first step in determining how the innate immune response will be shaped; yet the mechanisms that regulate this interaction remain largely unknown. In this study, we investigated the early cellular events triggered in macrophages in response to *Eh* and the putative virulent factors involved.

Methods: The cytoskeletal modulation of THP-1 macrophages was assessed by confocal microscopy and biochemical techniques following stimulation with *Eh* trophozoites. The contribution of *Eh* virulence factors and macrophage intracellular pathways and enzymes was evaluated with the use of specific inhibitors.

Results: We found that only live *Eh* in direct contact with human naive macrophages triggered an instantaneous degradation of the cytoskeletal-associated proteins Pyk2 and paxillin. This event was critically dependent on the major surface virulent factor, cysteine proteinase 5 (*Eh*CP5) as revealed using *Eh*CP5-deficient *Eh* and protease inhibitors. As macrophage cytoskeletal proteins are critically involved in cell adhesion, migration and inflammation, we surmise that *Eh* has evolved mechanisms to “stun” macrophages during infection to dampen the innate immune response.

Conclusion: Taken together, our findings advance a unique mechanism by which *Eh* modulates immune cells by interfering with the cell cytoskeleton, which may favour parasite colonization and/or altering pro-inflammatory responses in *Eh* pathogenesis.

Abstract 54

Kinematic gait patterns in individuals with mild-to-moderate hip osteoarthritis

Ryan Leigh¹, Sean Osis¹, and Reed Ferber¹

¹Faculty of Kinesiology, University of Calgary, Calgary, Alberta, Canada

Introduction: Hip osteoarthritis (OA) is a leading cause of pain and loss of function in affected individuals. Understanding the precise walking mechanics in non-surgical hip OA patients may provide valuable insight on how to clinically manage this population. Therefore, the purpose of the present study was to provide a comprehensive description of gait kinematics in individuals with radiographic evidence of mild-to-moderate hip OA as compared with matched controls.

Methods: 23 individuals with mild-to-moderate radiographic hip OA (as per the criteria of the American College of Rheumatology) and 22 healthy age and BMI matched subjects participated. Kinematic gait data were collected using an 8-camera 3D motion capture system (Vicon, Mx). Joint angles were calculated using the decomposition methods of Soderqvist et al. (1993). Peak joint angles were obtained in all three planes (sagittal, frontal, transverse) across the pelvis, hip, knee, and ankle during mid-stance (the time point corresponding to 30% of the gait cycle), terminal hip extension, and toe off of the affected side hip.

Mean differences in gait kinematics between groups was calculated using a two-way repeated measures ANOVA with group and time as the independent variables.

Results: Significant differences were observed between groups. Hip OA subjects hiked their unsupported hemi-pelvis compared with controls (CON: 0.76° (1.46) drop; HOA: 0.64° hike, $P=0.00$) and demonstrated an increased anterior pelvic tilt compared with controls (CON: 0.79° (3.50); HOA: 3.86° (3.64), $P=0.01$). Across the hip, OA patients demonstrated increased peak hip abduction (CON: 2.64° (3.59) adduction; HOA: 1.66° (3.50) abduction, $P=0.00$) and decreased peak hip extension (CON: 12.53° (7.05); HOA 3.96° (5.77), $P=0.00$).

Conclusion: Individuals with hip OA demonstrated significantly altered walking gait biomechanics as compared to healthy controls. These adaptations may be considered by clinicians working with this population. Understanding the under-

lying patho-anatomic changes that lead to these changes requires further investigation.

Abstract 55

Hierarchical difference in active and passive force production at long lengths in skeletal muscle

Brandon Hisey^{1,2} and Walter Herzog²

¹Cumming School of Medicine, University of Calgary; ²Human Performance Laboratory, University of Calgary, Calgary, Alberta, Canada

Introduction: According to the sliding filament and cross-bridge theories of contraction, the amount of active force produced by a muscle is dependent upon the overlap of the myofilaments actin and myosin. As muscle length increases, filament overlap decreases and therefore active force decreases while passive forces become greater. However, Leonard *et al.* (2010) showed that activated myofibrils stretched to lengths beyond myofilament overlap produce much higher forces than myofibrils stretched passively. This observation cannot be explained under the current framework of muscle contraction. The purpose of this study was to examine how this phenomenon scales to higher levels of muscle hierarchy. It was hypothesized that the divergence in active and passive force with increasing length would be reduced in isolated fibres, and further diminished in whole muscles.

Methods: Three separate preparations from the semitendinosus muscle of the frog *Rana pipiens* were used: whole muscles, skinned fibres, and myofibrils. Muscles were positioned at the optimal length of their force-length relationships and then stretched until failure, defined by a drop in force during stretch. Force and length data were collected throughout the stretch protocol, and forces at discrete sarcomere lengths were calculated.

Results: A two- to three-fold augmentation in active stress above the passive stress was observed in myofibrils stretched beyond myofilament overlap. Moving up in hierarchical level to isolated fibres and whole muscles resulted in progressive decreases in the difference between active and passive conditions at long sarcomere lengths. We suggest that at the myofibrillar level, the protein titin plays a crucial role in modulating force at long sarcomere lengths. As higher structural levels are exam-

ined, effects of passive structural elements outside the cell may mask some of the effects observed at subcellular levels.

Conclusion: The large divergence between active and passive stresses observed in myofibrils does not occur at higher levels of muscle hierarchy.

Abstract 56

Cost-free tools for managing dietary sodium in primary care: a Family Medicine Clerkship Community Health Challenge project

Lana Myroniuk¹ and Sakina Raj¹

¹Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

Background: Hypertension (HTN) is common in primary care, and it carries with it significant morbidity and mortality. Dietary sodium is a modifiable risk factor for the development of HTN, however Canadian sodium intake often doubles the recommended 1500 mg/day due to poor health literacy, the prevalence of processed foods in the North American diet, and individual cooking practices.

Case Presentation: The Ranchlands Medical Clinic is a primary care clinic located in northwest Calgary, AB, serving a diverse population. Many of these patients have poor food literacy and consume high levels of dietary sodium, placing them at risk for developing HTN. A brief literature search through PubMed Clinical Queries containing the phrase “sodium + hypertension + primary care” (Category: Therapy; Scope: Narrow) revealed current evidence-based methods to reduce sodium intake include intense nutrition counseling, funded cooking lessons, and pre-prepared low-sodium meals for patients with HTN. However, these are not feasible methods of managing dietary sodium, as primary care clinics seldom have the time, financial, or staff resources to sustain these interventions. An investigation to identify free sodium education resources was launched. The results include print and online resources published by Alberta Health Services (AHS), Government of Canada, and Dietitians of Canada (DC). These free resources can be followed up with periodic physician office visits to improve motivation/accountability in patients with or at risk for developing HTN.

Conclusion: The combination of empowering patients with cost-free, take-home resources and periodic follow-up is a realistic and sustainable approach to managing dietary sodium in primary care clinics. Patients and physicians have been receptive to this model at the Ranchlands Medical Clinic thus far.

Abstract 57

Investigating the Perceptions and Satisfaction Outcomes of Women Receiving Intrauterine Devices

Paige Hacking¹, Shaye Lafferty¹, and Rupinder Mangat^{1,2}

¹Cumming School of Medicine, University of Calgary, Calgary; ²Northeast Calgary Women's Clinic and the IUD Clinic, Calgary, Alberta, Canada

Introduction: More women are choosing intrauterine devices (IUDs) as their preferred form of birth control. In response to this, additional information needs to be gathered to characterize this trend so as to better equip healthcare professionals in counselling their patients. This study aimed to determine the demographics and patient experiences of women receiving IUDs.

Methods: Female patients of The IUD Clinic in Calgary attending their six-week IUD post-insertion appointments were eligible to complete optional and anonymous surveys entitled the “IUD Experience Survey”. Surveys explored patient demographics, previous vaginal delivery, pre-insertion misoprostol use, reported insertion pain, and overall satisfaction with IUD choice. All rating scales were evaluated using a 5-point Likert scale.

Results: Of the 128 women who received surveys, 85% fully completed the questions used for outcome analysis. The average age of participants was 30 years old. The reported relationship statuses included dating regular partner (36%), living with regular partner (34%), married (36%), and no regular partner (9%). The top cited reason for switching from their previous contraceptive method to an IUD was “trouble remembering to take/use birth control”. There was a statistically significant decrease in reported pain in patients who gave a history of prior vaginal delivery (2.52 ± 0.22) compared to those who did not (3.71 ± 0.13). The use of misoprostol prior to insertion did not produce a statistically significant difference in reported pain. The participants' overall satisfaction rating of their IUD was 4.13 ± 0.07 .

Conclusion: Prior vaginal delivery appears to be associated with a less painful insertion; however, it is unclear as to whether misoprostol has an effect in decreasing pain. Despite painful insertions, participants were very satisfied with their IUD choice. With these findings, physicians will be better informed when counselling their patients on what to expect in choosing an IUD.